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File 350:Derwent WPIX 1963-2004/UD,UM &UP=200434
File 347:JAPIO Nov 1976-2004/Jan(Updated 040506)
File 371:French Patents 1961-2002/BOPI 200209
File 348:EUROPEAN PATENTS 1978-2004/May W04
File 349:PCT FULLTEXT 1979-2002/UB=20040527,UT=20040520
S1          51   AU='PETTIS R' OR AU='PETTIS R J' OR AU='PETTIS RONALD' OR -
               AU='PETTIS RONALD J'
S2          46   AU='DOWN J' OR AU='DOWN J A' OR AU='DOWN JAMES' OR AU='DOWN
               JAMES A' OR AU='DOWN JAMES ARTHUR'
S3          33   AU='HARVEY N' OR AU='HARVEY N A' OR AU='HARVEY NOEL' OR AU-
               ='HARVEY NOEL G' OR AU='HARVEY NOEL GRAY'
S4           6   S1 AND S2 AND S3
S5       21315   INTRADERMAL?
S6          25   (S1:S3 AND S5) NOT S4
S7          25   IDPAT (sorted in duplicate/non-duplicate order)
S8          16   IDPAT (primary/non-duplicate records only)

4/3,AB/6      (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00860693
SKIN PERMEABILITY ENHANCING DEVICE TO WITHDRAW OR ADMINISTER A SUBSTANCE
    AND METHOD OF MANUFACTURING THE DEVICE
DISPOSITIF RENFORCANT LA PERMEABILITE DE LA PEAU POUR RETIRER OU
    ADMINISTRER UNE MATIERE ET PROCEDE DE FABRICATION DU DISPOSITIF
Patent Applicant/Assignee:
  BECTON DICKSON AND COMPANY, Intellectual Property Department, Mail Code
    089, 1 Becton Drive, Franklin Lakes, NJ 07417-1880, US, US (Residence),
    US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
   DOWN James , 814 Oakley Court, Cary, NC 27511, US, US (Residence), US
    (Nationality), (Designated only for: US)
   HARVEY Noel G , 3211 US 70 West, Efland, NC 27243, US, US (Residence),
    US (Nationality), (Designated only for: US)
  MARTIN Frank E, 2807 Burton Road, Durham, NC 27704, US, US (Residence),
    US (Nationality), (Designated only for: US)
   PETTIS Ronald J , 529 Darby Glen Lane, Durham, NC 27713, US, US
    (Residence), US (Nationality), (Designated only for: US)
  LASTOVICH Alexander G, 8800 Klondike Court, Raleigh, NC 27615, US, US
    (Residence), US (Nationality), (Designated only for: US
Legal Representative:
  SCHMIDT Richard D (et al) (agent), Venable, Baetjer, Howard & Civiletti,
    LLP, 1201 New York Avenue, NW, Suite 1000, P.O. Box 34385, Washington,
    DC 20043-9998, US,
Patent and Priority Information (Country, Number, Date):
  Patent:              WO 200193946 A1 20011213 (WO 0193946)
  Application:         WO 2001US18531 20010608  (PCT/WO US0118531)
  Priority Application: US 2000590062 20000608
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ
  DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
  LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
  SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
  (EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
  (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
  (AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
  (EA) AM AZ BY KG KZ MD RU TJ TM
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Publication Language: English
Filing Language: English
Fulltext Word Count: 6651
English Abstract

A device includes a plurality of skin penetrating devices for delivering or withdrawing a substance through the skin of a patient. The device has a support formed with a top and bottom end and a plurality of channels extending axially through the support. A plurality of the skin penetrating members is positioned in the channels with a tip extending from the bottom end of the support. A coupling member is attached to the support for coupling with a fluid supply and directing the fluid to the skin penetrating members. The skin penetrating members have a length of about 100 microns to about 2000 microns and are about 30 to 50 gauge.

8/3,AB,IC/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016099476
WPI Acc No: 2004-257352/200424
XRAM Acc No: C04-100586
XRPX Acc No: N04-204526

Direct delivery of immunomodulatory substance into intradermal **space within mammalian skin involves administering the substance through hollow needles having outlet with specific exposed height**

Patent Assignee: PETTIS R J (PETT-I); BECTON DICKINSON & CO (BECT)
Inventor: **PETTIS R J**
Number of Countries: 105 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200420014	A2	20040311	WO 2003US26750	A	20030828	200424 B
US 20040082934	A1	20040429	US 2002406916	P	20020830	200429
			US 2003650039	A	20030828	

Priority Applications (No Type Date): US 2002406916 P 20020830; US 2003650039 A 20030828
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200420014	A2	E	36	A61M-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

US 20040082934 A1 A61M-031/00 Provisional application US 2002406916
Abstract (Basic): WO 200420014 A2
Abstract (Basic):

NOVELTY - An immunomodulatory substance is directly delivered into an **intradermal** space within mammalian skin by administering the substance through hollow needle(s) having an outlet with an exposed height of 0-1 mm so that the delivery of the substance occurs at a depth of 0.3-2 mm. The outlet is inserted into the skin to a depth of 0.3-2 mm.

USE - For directly delivering an immunomodulatory substance into an **intradermal** space within mammalian skin.

ADVANTAGE - The invention produces efficacious results in comparison with the administration to either space by itself, readily reaches the richly vascularized papillary dermis, is rapidly absorbed into the blood capillaries and/or lymphatic vessels to become systemically bioavailable, achieves more rapid systemic distribution and offset of administered substances and higher bioavailabilities of administered substances, and attains higher maximum concentrations of administered substances. The substances administered are absorbed more rapidly, with bolus administration resulting in higher initial administration.

pp; 36 DwgNo 0/1

International Patent Class (Main): A61M-000/00; A61M-031/00

8/3,AB,IC/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX

015854188

WPI Acc No: 2004-012020/200401

Related WPI Acc No: 2003-748103; 2004-364815

XRAM Acc No: C04-003640

Delivery of therapeutic substance to subject, by delivering the substance within or beneath skin into intradermal **space to access compartments that** afford the substance different pharmakinetics

Patent Assignee: GINSBERG B (GINS-I); HARVEY N (HARV-I); PETTIS R J (PETT-I); BECTON DICKINSON & CO (BECT)

Inventor: GINSBERG B; **HARVEY N** ; **PETTIS R J** ; HARVEY N G

Number of Countries: 103 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200394995	A1	20031120	WO 2003US14063	A	20030506	200401 B
US 20040023844	A1	20040205	US 2002377649	P	20020506	200411
			US 2002389881	P	20020620	
			US 2003429973	A	20030506	

Priority Applications (No Type Date): US 2002389881 P 20020620; US 2002377649 P 20020506; US 2003429973 A 20030506

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200394995	A1	E	36	A61M-001/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

US 20040023844 A1 A61K-031/00 Provisional application US 2002377649
Provisional application US 2002389881

Abstract (Basic): WO 200394995 A1

Abstract (Basic):

NOVELTY - Therapeutic substance is delivered to a subject by delivering the substance within or beneath the skin at least into an **intradermal** space to access at least two compartments that afford the substance different pharmakinetics.

USE - The method is for delivering a therapeutic substance to a subject.

ADVANTAGE - The inventive method provides systemic absorption of the substances to the skin and improved pharmakinetics based on biphasic or bimodel kinetic profiling. It enhances the effectiveness of the substance in terms of a resultant composite pharmakinetics compared to delivery to a single compartment. It provides rapid and high peak onset levels of the compound and lower prolonged circulating level of the compound.

DESCRIPTION OF DRAWING(S) - The figure shows the average glucose concentration over time after delivery of insulin into skin at two different **intradermal** depths and one subcutaneous depth.

pp; 36 DwgNo 1/7

International Patent Class (Main): A61K-031/00; A61M-001/00
International Patent Class (Additional): A61M-031/00

8/3,AB,IC/3 (Item 3 from file: 350)

DIALOG(R)File 350:Derwent WPIX
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015748430
WPI Acc No: 2003-810631/200376
Related WPI Acc No: 2001-275185; 2002-138770; 2002-147984; 2002-147985; 2002-453736; 2002-488657; 2002-656032; 2003-046890; 2003-058613; 2003-092966; 2003-401429; 2003-596285; 2003-596286; 2003-708201; 2004-010389
XRAM Acc No: C03-225099
XRPX Acc No: N03-649056

Therapeutic substance reduction method for medical applications involves inserting outlet of small gauge hollow needle

Patent Assignee: BECTON DICKINSON & CO (BECT); HARVEY N G (HARV-I); ALCHAS P G (ALCH-I); DOWN J (DOWN-I); PETTIS R J (PETT-I)
Inventor: ALCHAS P G; **DOWN J A** ; **PETTIS R J** ; **DOWN J** ; HARVEY N G
Number of Countries: 102 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020156453	A1	20021024	US 99417671	A	19991014	200376 B
			US 2000606909	A	20000629	
			US 2001835243	A	20010413	
			US 2001893746	A	20010629	
			US 200128989	A	20011228	
WO 200357143	A2	20030717	WO 2002US40841	A	20021223	200376
AU 2002360693	A1	20030724	AU 2002360693	A	20021223	200421

Priority Applications (No Type Date): US 200128989 A 20011228; US 99417671 A 19991014; US 2000606909 A 20000629; US 2001835243 A 20010413; US 2001893746 A 20010629
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020156453	A1		24	A61M-031/00	CIP of application US 99417671
					CIP of application US 2000606909
					CIP of application US 2001835243
					CIP of application US 2001893746
WO 200357143	A2	E		A61K-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB

GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
AU 2002360693 A1 A61M-031/00 Based on patent WO 200357143
Abstract (Basic): US 20020156453 A1
Abstract (Basic):
NOVELTY - A method for reducing the amount of bioactive substance administered to a patient achieving a therapeutic or diagnostic effect.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for treatment of a symptom of a pathological condition.
USE - For reduction of therapeutic substance for administration of substances in the **intradermal** layer of skin.
ADVANTAGE - Since the outlet of small gauge hollow needle is inserted into skin, at predetermined depth to deliver the substance to the predetermined depth, the substance are safely, more efficiently and accurately delivered without any leakage.
DESCRIPTION OF DRAWING(S) - The figure shows the time course of plasma insulin level of **intradermal** versus subcutaneous bolus administration of fast acting.
pp; 24 DwgNo 1/10
International Patent Class (Main): A61K-000/00; A61M-031/00

8/3,AB,IC/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015553763
WPI Acc No: 2003-615918/200358
XRAM Acc No: C03-168015
XRPX Acc No: N03-490406
Device for intradermally **delivering or withdrawing substance through the skin of a patient, comprises body having bottom and top faces, side edge and width, and skin penetrating device**
Patent Assignee: CONNELLY R I (CONN-I); PETTIS R J (PETT-I); BECTON DICKINSON & CO (BECT)
Inventor: CONNELLY R I; **PETTIS R J**
Number of Countries: 101 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 20030069548	A1	20030410	US 2001971145	A	20011005	200358	B
WO 200330984	A1	20030417	WO 2002US31807	A	20021004	200358	
US 6689100	B2	20040210	US 2001971145	A	20011005	200413	

Priority Applications (No Type Date): US 2001971145 A 20011005
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20030069548	A1		13	A61M-005/00	
WO 200330984	A1	E		A61M-031/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
US 6689100 B2 A61M-005/00
Abstract (Basic): US 20030069548 A1
Abstract (Basic):
NOVELTY - A device for **intradermally** delivering or withdrawing a substance through the skin of a patient, comprises a body having bottom

face (BF), top face (TF), side edge and width, and skin penetrating device coupled to BF. The body forms a channel extended longitudinally from edge, which is substantially parallel to BF. The skin penetrating device is joined with fluid channel..

DETAILED DESCRIPTION - A device for **intradermally** delivering or withdrawing a substance through layer(s) of the skin of patient, comprises a body having bottom face (BF), top face (TF) spaced from BF, side edge and width, and skin penetrating device coupled to BF. The body has lower height extending between TF and BF than width. The body forms a channel extended longitudinally from edge, which is substantially parallel to BF. The skin penetrating device is joined with fluid channel.

INDEPENDENT CLAIMS are also included for:

(1) a method for delivering or withdrawing substance through layer of skin of patient; and

(2) a micro device interface.

USE - For delivering or withdrawing substance such as pharmaceutical agents such as drugs e.g. antibiotics, antiviral agents, analgesics, anesthetics, antiarthritics, antidepressants, antihistamines, anti-inflammatory agents, and vaccines, through a layer such as below the stratum corneum of skin of patient.

ADVANTAGE - The device can remain in contact with the skin for sufficient time to withdraw from or deliver the desired substances to the patient. The device is disposable and single-use device. The device is particularly suitable for introducing a vaccine **intradermally** e.g. for efficiently delivering a small amount of a vaccine antigen. The device enhances the penetration of a micro needle array. The structure of the device provides a low profile and an increased comfort level to the patient. The device can be easily manufactured as a single piece by injection molding.

DESCRIPTION OF DRAWING(S) - The figure shows an exploded view of the device.

device (10)
body (12)
skin penetrating device (14)
top face (18)
bottom face (20)
fluid channels (24,26)
pp; 13 DwgNo 2/13

International Patent Class (Main): A61M-005/00; A61M-031/00
International Patent Class (Additional): A61K-009/22; A61M-005/32; A61M-035/00

8/3,AB,IC/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX

015386851
WPI Acc No: 2003-447796/200342
XRAM Acc No: C03-118969
XRPX Acc No: N03-357111

Microneedle delivery device for delivery of substance, e.g. medications, to intraepidermal space, has hub housing and piercing member for piercing substance supply reservoir and communicate it with microneedle

Patent Assignee: KAESTNER S A (KAES-I); MARTIN F E (MART-I); PETTIS R J (PETT-I); BECTON DICKINSON & CO (BECT)
Inventor: KAESTNER S A; MARTIN F E; **PETTIS R J** ; KAESTNER S; MARTIN F;

PETTIS R

Number of Countries: 101 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 20030050602	A1	20030313	US 2001318886	P	20010912	200342	B
			US 2001318913	P	20010912		
			US 2002238958	A	20020911		
WO 200322330	A2	20030320	WO 2002US28785	A	20020911	200342	

Priority Applications (No Type Date): US 2002238958 A 20020911; US 2001318886 P 20010912; US 2001318913 P 20010912
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20030050602	A1		18	A61M-005/00	Provisional application US 2001318886 Provisional application US 2001318913
WO 200322330	A2	E		A61M-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

Abstract (Basic): US 20030050602 A1

Abstract (Basic):

NOVELTY - A microneedle delivery device includes a hub housing having proximate end with coupling member for coupling the device to a supply reservoir containing a substance to be delivered to a patient; and a piercing member for piercing the supply reservoir and communicate the substance to a microneedle. The microneedle penetrates the skin of the patient.

DETAILED DESCRIPTION - A microneedle delivery device includes a hub (16) housing (24) having proximate end with coupling member for coupling the device to a supply reservoir containing a substance to be delivered to a patient, and a distal end having a skin contact surface (26); and a piercing member at the proximate end and is for piercing the supply reservoir and communicate the substance to a microneedle (14). The microneedle is attached to and extending from the skin contact surface. It penetrates the skin of the patient to a selected depth.

An INDEPENDENT CLAIM is also included for method for **intradermal** delivery of a substance by engaging a hub assembly, piercing a septum of the cartridge in the housing, controlling the housing to insert the microneedle at the insertion site on a patient, and controlling the mechanism within the housing.

USE - The device is for the delivery of substances, e.g. medications, to intraepidermal, **intradermal** , or shallow subcutaneous space.

ADVANTAGE - The invention allows effective communication of the cartridge contents via the microneedle patient interface. Specifically, it allows ready transport of liquid or suspension from a cartridge to the microneedle inlet, without requiring excessive pressure or occlusion. It allows accurately accesses the desired tissue depth in the skin. It can be maintained in an orientation or configuration with respect to the patient's skin for sufficient time period to accomplish delivery.

DESCRIPTION OF DRAWING(S) - The figure is a perspective view of

single microneedle hub assembly.
Tensioning member (12)
Microneedle (14)
Hub (16)
Housing (24)
Contact surface (26)
Engagement opening (30)
Hub opening (32)
pp; 18 DwgNo 1A/6
International Patent Class (Main): A61M-000/00; A61M-005/00

8/3,AB,IC/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015032449
WPI Acc No: 2003-092966/200308
Related WPI Acc No: 2001-275185; 2002-147984; 2002-147985; 2002-188692; 2002-656032; 2003-046890; 2003-058613; 2003-401429; 2003-689556; 2003-810631
XRAM Acc No: C03-023213
XRPX Acc No: N03-073782
Directly delivering a high molecular weight substance into an intradermal **space within mammalian skin, comprises administering the substance through hollow needles by injecting to a specified depth in the skin**
Patent Assignee: BECTON DICKINSON & CO (BECT); MIKSZTA J A (MIKS-I); PETTIS R J (PETT-I); SUTTER D E (SUTT-I)
Inventor: KAESTNER S A; MIKSZTA J A; **PETTIS R J** ; SUTTER D E
Number of Countries: 101 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200283231	A1	20021024	WO 2001US50436	A	20011228	200308 B
EP 1381422	A1	20040121	EP 2001992390	A	20011228	200410
			WO 2001US50436	A	20011228	
AU 2002232860	A1	20021028	AU 2002232860	A	20011228	200433

Priority Applications (No Type Date): US 2001893746 A 20010629; US 2001835243 A 20010413
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200283231	A1	E	39	A61M-037/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

EP 1381422	A1	E	A61M-037/00	Based on patent WO 200283231

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

AU 2002232860	A1	A61M-037/00	Based on patent WO 200283231

Abstract (Basic): WO 200283231 A1
Abstract (Basic):
NOVELTY - Directly delivering a high molecular weight substance into an **intradermal** space within mammalian skin, comprises administering the substance through a hollow needle having an outlet with an exposed height between 0 - 1 mm, into the skin to a depth of

0.3 - 2 mm.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a microneedle for **intradermal** injection for delivering a high molecular weight substance into the dermis, where the microneedle has a length and outlet selected for its suitability for specifically delivering the substance into the dermis; and

(2) delivering a bioactive substance to a subject, by contacting the skin with a device having a dermal-access unit for accurately targeting the dermal space of the subject with bioactive substance.

USE - The method is used for administering a high molecular weight substance, such as, a protein, hormone or nucleic acid, into an **intradermal** space within mammalian skin (claimed).

ADVANTAGE - The method provides more rapid onset effect of drugs and diagnostic substances than subcutaneous administration of drugs. Natural hormones are released in pulsatile fashion with a rapid onset burst followed by rapid clearance. The **intradermal** administered drug readily reaches the richly vascularized papillary dermis and is rapidly absorbed into the blood capillaries and/or lymphatic vessels effectively. The **intradermal** administration results in enhanced bioavailability by using less drug. This results in direct economic benefit to the manufacturer and to the consumer, especially for expensive protein therapeutics and diagnostics. Hence, higher bioavailability with reduced dosing rates results in higher beneficial effects to the patient, without producing side effects. The dermal-access unit prevents the leakage of the substance from the skin and improves absorption within the **intradermal** space effectively. The microneedle has a very sharp and very small gauge, hence it reduces pain and other sensations during injection or infusion. The microneedles are assembled or fabricated in linear arrays or two dimensional arrays to increase the rate of delivery or the amount of substance delivered in a given period of time. The delivery and volume is also controlled to prevent the formation of wheals at the site of delivery and to prevent back pressure from pushing the dermal-access unit out of the skin.

pp; 39 DwgNo 1/1

International Patent Class (Main): A61M-037/00
International Patent Class (Additional): A61B-017/20; A61M-005/46

8/3,AB,IC/7 (Item 7 from file: 350)

DIALOG(R)File 350:Derwent WPIX

014998098
WPI Acc No: 2003-058613/200305
Related WPI Acc No: 2001-275185; 2002-147984; 2002-147985; 2002-188692; 2002-656032; 2003-046890; 2003-092966; 2003-401429; 2003-689556; 2003-810631
XRAM Acc No: C03-015105
XRPX Acc No: N03-045406

Delivery of a substance into an intradermal **layer of skin involves bolus administration of the substance into the dermis**

Patent Assignee: BECTON DICKINSON & CO (BECT); KAESTNER S A (KAES-I); PHARMACIA & UPJOHN (PHAA); ALCHAS P G (ALCH-I); DOWN J A (DOWN-I); HARVEY N G (HARV-I); PETTIS R J (PETT-I)
Inventor: GARBERG P; KAESTNER S A; MIKSZTA J A; **PETTIS R J** ; PINKERTON T C ; STRAUSS P; SUTTER D E; WESTERBERG G; ALCHAS P G; **DOWN J A** ; HARVEY N G

Number of Countries: 101 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200283232	A1	20021024	WO 2001US50440	A	20011228	200305 B
US 20030100885	A1	20030529	US 99417671	A	19991014	200337
			US 2001835243	A	20010413	
			US 2001301531	P	20010629	
			US 2001893746	A	20010629	
			US 200128988	A	20011228	
EP 1381423	A1	20040121	EP 2001992391	A	20011228	200410
			WO 2001US50440	A	20011228	
AU 2002232861	A1	20021028	AU 2002232861	A	20011228	200433

Priority Applications (No Type Date): US 2001893746 A 20010629; US 2001835243 A 20010413; US 2001301531 P 20010629; US 99417671 A 19991014; US 200128988 A 20011228
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200283232	A1	E	60	A61M-037/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

US 20030100885	A1	A61M-005/32	CIP of application US 99417671
			CIP of application US 2001835243
			Provisional application US 2001301531
			CIP of application US 2001893746
			CIP of patent US 6494865
EP 1381423	A1 E	A61M-037/00	Based on patent WO 200283232

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

AU 2002232861	A1	A61M-037/00	Based on patent WO 200283232

Abstract (Basic): WO 200283232 A1
Abstract (Basic):

NOVELTY - Direct delivery of a substance into an **intradermal**0 space within a mammal involves bolus administration of the substance into the dermis. The administered substance has at least one improved pharmacokinetic parameter relative to the same parameter produced on administration of the same substance subcutaneously.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for delivering a bioactive substance to a subject involving contacting the skin with a device having dermal access source for accurately targeting the dermal space with bioactive substance.

USE - For directly administering human growth hormone, polysaccharide, heparin molecule or its fragment having anticoagulant activity, Fragmin (RTM), protein, Genotropin (RTM) and pegylated protein into the **intradermal** layer of the skin in mammals for systemic absorption (claimed).

ADVANTAGE - The method is efficient and safe. The method achieves more rapid systemic distribution and offset of drugs or diagnostic agents, higher bioavailabilities and attains higher maximum concentrations of drugs or diagnostic substances. There is no change in systemic elimination rates or intrinsic clearance mechanisms of drugs or diagnostic substances and in pharmacodynamic or biological response

mechanisms. The method removes the physical or kinetic barriers invoked when drugs pass through and become trapped in cutaneous tissue compartments prior to systemic absorption. The method has highly controllable dosing regimens and reduced degradation of drugs and diagnostic agents and/or undesirable immunogenic activity. The method achieves decrease in Tmax (time to achieve maximum blood concentration of drug), Tlag (lag time) and increase in Cmax (maximum concentration of dose). The method enhanced absorption rate, rapid onset of pharmacodynamics or biological effects, and reduced drug depot effects. The method takes substantially shorter time to reach a threshold blood serum concentration as compared with the subcutaneous administration of the substance at an identical dose and rate of delivery.

pp; 60 DwgNo 0/11

International Patent Class (Main): A61M-005/32; A61M-037/00
International Patent Class (Additional): A61B-017/20; A61M-005/46

8/3,AB,IC/8 (Item 8 from file: 350)

DIALOG(R)File 350:Derwent WPIX

014835326
WPI Acc No: 2002-656032/200270
Related WPI Acc No: 2001-275185; 2002-138770; 2002-147984; 2002-147985; 2002-453736; 2002-488657; 2003-046890; 2003-058613; 2003-092966; 2003-401429; 2003-596285; 2003-596286; 2003-708201; 2003-810631; 2004-010389
XRAM Acc No: C02-184164
XRPX Acc No: N02-518494

Delivery of bioactive substance to subject, involves using device having dermal-access mechanism

Patent Assignee: ALCHAS P G (ALCH-I); DOWN J (DOWN-I); HARVEY N G (HARV-I); PETTIS R J (PETT-I)
Inventor: ALCHAS P G; **DOWN J**; HARVEY N G; **PETTIS R J**
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020095134	A1	20020718	US 99417671	A	19991014	200270 B
			US 2000606909	A	20000629	
			US 2001835243	A	20010413	
			US 2001893746	A	20010629	

Priority Applications (No Type Date): US 2001893746 A 20010629; US 99417671 A 19991014; US 2000606909 A 20000629; US 2001835243 A 20010413
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020095134	A1		23	A61M-031/00	CIP of application US 99417671
					CIP of application US 2000606909
					CIP of application US 2001835243

Abstract (Basic): US 20020095134 A1
Abstract (Basic):

NOVELTY - A bioactive substance is delivered to a subject by contacting the subject's skin with a device having dermal-access mechanism for accurately targeting the dermal space of the subject with the bioactive substance.

USE - For delivering bioactive or pharmaceutical substance, e.g. peptide or protein (such as insulin, granulocyte stimulating factor, or parathyroid hormone), or nucleic acid, to a subject.

ADVANTAGE - The use of dermal-access mechanism provides a readily

accessible and reproducible parenteral delivery route with high bioavailability and ability to modulate plasma profiles. It enables efficient migration of substance to the vascular and lymphatic microcapillary bead. It achieves more rapid systemic distribution and offset of drugs or diagnostic agents. The delivered substance has improved pharmacokinetics (i.e. increased bioavailability, decreased Tmax, increased Cmax, decreased Tlag, and enhanced absorption rate) compared to pharmacokinetics of substance after subcutaneous injection.

DESCRIPTION OF DRAWING(S) - The figure shows a time course of plasma insulin levels of **intradermal** versus subcutaneous bolus administration.

pp; 23 DwgNo 1/10

International Patent Class (Main): A61M-031/00

8/3,AB,IC/9 (Item 9 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014667953
WPI Acc No: 2002-488657/200252
Related WPI Acc No: 2001-275185; 2002-138770; 2002-453736; 2002-656032; 2003-046890; 2003-401429; 2003-596285; 2003-596286; 2003-708201; 2003-810631; 2004-010389
XRAM Acc No: C02-138760
XRPX Acc No: N02-386208

Making of intradermal **injection into animal skin uses drug delivery device containing substance to be injected**

Patent Assignee: BECTON DICKINSON & CO (BECT); MIKSZTA J A (MIKS-I); PETTIS R J (PETT-I); SUTTER D E (SUTT-I); KAESTNER S A (KAES-I); PHARMACIA & UPJOHN (PHAA); ALCHAS P G (ALCH-I); FERNAND LAURENT P E (LAUR-I)

Inventor: KAESTNER S A; GARBERG P; MIKSZTA J A; **PETTIS R J** ; PINKERTON T C ; STRAUSS P; SUTTER D E; WESTERBERG G; ALCHAS P G; FERNAND LAURENT P E; LAURENT P E F

Number of Countries: 002 Number of Patents: 004

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020038111	A1	20020328	US 99417671	A	19991014	200252 B
			US 2001835243	A	20010413	
US 6569143	B2	20030527	US 99417671	A	19991014	200337
			US 2001835243	A	20010413	
AU 2002232861	A1	20021028	AU 2002232861	A	20011228	200433
AU 2002232860	A1	20021028	AU 2002232860	A	20011228	200433

Priority Applications (No Type Date): US 2001835243 A 20010413; US 99417671 A 19991014; US 2001893746 A 20010629; US 2001301531 P 20010629

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020038111	A1		18	A61M-005/00	CIP of application US 99417671
US 6569143	B2			A61M-031/00	CIP of application US 99417671
AU 2002232861	A1			A61M-037/00	Based on patent WO 200283232
AU 2002232860	A1			A61M-037/00	Based on patent WO 200283231

Abstract (Basic): US 20020038111 A1

Abstract (Basic):

NOVELTY - An **intradermal** injection is made into an animal skin by using a drug delivery device containing a substance to be injected.

DETAILED DESCRIPTION - Making of **intradermal** injection into an animal skin involves:

(i) providing a drug delivery device including a needle cannula having a forward needle tip, where needle cannula is in fluid communication with a substance obtained in the drug delivery device and including a limiter portion surrounding the needle cannula and limiter portion includes a skin engaging surface (42) with the needle tip of the needle cannula extending from the limiter portion beyond the skin engaging surface at a distance of 0.5-3 mm and the needle cannula has a fixed angle of orientation relative to a plane of the skin engaging surface of the limiter portion;

(ii) inserting the needle tip into the skin of an animal and engaging the surface of the skin with the skin engaging surface of the limiter portion such that the skin engaging surface of the limiter portion limits penetration of the needle tip into a dermis layer of the animal skin; and

(iii) expelling the substance from the device through the needle tip into the skin animal.

USE - For making an **intradermal** injection into the animal skin.

ADVANTAGE - The invented method effectively and reliably delivers substances **intradermally** .

pp; 18 DwgNo 0/10

International Patent Class (Main): A61M-005/00; A61M-031/00; A61M-037/00
International Patent Class (Additional): A61B-017/20; A61M-005/46

8/3,AB,IC/10 (Item 10 from file: 350)

DIALOG(R)File 350:Derwent WPIX
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014351059
WPI Acc No: 2002-171762/200222
XRAM Acc No: C02-053189
XRPX Acc No: N02-130571

Manufacture of microdevice for delivering or withdrawing substance through patient's skin, by positioning skin penetrating device in recessed area of support, and applying bonding agent to wick between base and support

Patent Assignee: BECTON DICKINSON & CO (BECT); EVANS J D (EVAN-I); LASTOVICH A G (LAST-I); PETTIS R J (PETT-I)
Inventor: EVANS J D; LASTOVICH A G; **PETTIS R J**
Number of Countries: 097 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200205890	A2	20020124	WO 2001US21791	A	20010711	200222	B
AU 200173340	A	20020130	AU 200173340	A	20010711	200236	
US 6440096	B1	20020827	US 2000616771	A	20000714	200259	
US 20020183688	A1	20021205	US 2000616771	A	20000714	200301	
			US 2002192474	A	20020710		
EP 1301237	A2	20030416	EP 2001952607	A	20010711	200328	
			WO 2001US21791	A	20010711		
JP 2004503342	W	20040205	WO 2001US21791	A	20010711	200412	
			JP 2002511820	A	20010711		

Priority Applications (No Type Date): US 2000616771 A 20000714; US 2002192474 A 20020710
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200205890	A2	E	29	A61M-037/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ

PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
AU 200173340 A A61M-037/00 Based on patent WO 200205890
US 6440096 B1 A61N-001/30
US 20020183688 A1 A61M-001/00 Cont of application US 2000616771
Cont of patent US 6440096
EP 1301237 A2 E A61M-037/00 Based on patent WO 200205890
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT
LI LT LU LV MC MK NL PT RO SE SI TR
JP 2004503342 W 46 A61M-037/00 Based on patent WO 200205890
Abstract (Basic): WO 200205890 A2
Abstract (Basic):

NOVELTY - A microdevice is manufactured by providing a support having a bottom face with a recessed area, positioning a skin penetrating device in the recessed area of the support, and applying a bonding agent between the support and the base in the recessed area. The penetrating device has a base and skin penetrating member(s). The bonding agent has a viscosity to wick between the base and support.

DETAILED DESCRIPTION - Manufacture of a microdevice comprises providing a support (12) having a bottom face with a recessed area having a dimension less than a dimension of a bottom face and positioning a skin penetrating device in the recessed area of the support. The skin penetrating device has a base and skin penetrating member(s). The base has a dimension less than the dimension of the recessed area. A bonding agent is applied to location between the support and the base in the recessed area. It has a viscosity to wick between the base and the support.

An INDEPENDENT CLAIM is also included for a device for delivering or withdrawing a substance, e.g. pharmaceutical agents or drugs from a patient comprising support member, skin penetrating device, and bonding material.

USE - The method is used for manufacturing microdevice for delivering or withdrawing a substance, e.g. pharmaceutical agents or drugs through the skin of a patient. The device introduces a vaccine **intradermally** for delivering vaccine antigen for presentation to the langerhans cells.

ADVANTAGE - The device is a disposable, single-use device. It can be used safely and effectively. It provides no pain to the patient when the device is penetrated to the skin.

DESCRIPTION OF DRAWING(S) - The figure is a perspective view of the sampling or delivery device.

Support (12)
Opening (28)
Flange (30)
pp; 29 DwgNo 1/12

International Patent Class (Main): A61M-001/00; A61M-037/00; A61N-001/30
International Patent Class (Additional): A61B-010/00; A61B-017/322

8/3,AB,IC/11 (Item 11 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014327282
WPI Acc No: 2002-147985/200219
Related WPI Acc No: 2001-275185; 2002-147984; 2002-188692; 2002-656032;
2003-046890; 2003-058613; 2003-092966; 2003-689556; 2003-810631

XRAM Acc No: C02-045978
XRPX Acc No: N02-112152

Direct delivery of substance into intradermal space within mammalian skin by administering the substance through at least one small gauge hollow needle with an outlet of predetermined height

Patent Assignee: BECTON DICKINSON & CO (BECT)
Inventor: **DOWN J A** ; NOEL H G; **PETTIS R J** ; HARVEY N G
Number of Countries: 097 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200202179	A1	20020110	WO 2001US20782	A	20010629	200219	B
AU 200170262	A	20020114	AU 200170262	A	20010629	200237	
EP 1296740	A1	20030402	EP 2001948832	A	20010629	200325	
			WO 2001US20782	A	20010629		
BR 200112313	A	20030624	BR 200112313	A	20010629	200343	
			WO 2001US20782	A	20010629		
CN 1438905	A	20030827	CN 2001811892	A	20010629	200375	
JP 2004501725	W	20040122	WO 2001US20782	A	20010629	200411	
			JP 2002506800	A	20010629		

Priority Applications (No Type Date): US 2000606909 A 20000629
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200202179	A1	E	47	A61M-037/00	
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW				
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
AU 200170262	A			A61M-037/00	Based on patent WO 200202179
EP 1296740	A1	E		A61M-037/00	Based on patent WO 200202179
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 200112313	A			A61M-037/00	Based on patent WO 200202179
CN 1438905	A			A61M-037/00	
JP 2004501725	W		73	A61M-037/00	Based on patent WO 200202179

Abstract (Basic): WO 200202179 A1
Abstract (Basic):

NOVELTY - Directly delivering a substance into an **intradermal** space within mammalian skin, comprising administering the substance through at least one small gauge hollow needle having an outlet with a height of 0-1 mm and inserting into the skin to a depth of 0.3-2 mm, so that delivery of the substance occurs at a depth of 0.3-2 mm, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a microneedle for **intradermal** injection of a pharmaceutical substance, which has a length and outlet selected for its stability for specifically delivering the substance into the dermis.

USE - For directly delivering a substance into an **intradermal** space within mammalian skin. The substance is a nucleic acid, a hormone, or a peptide or protein including insulin, granulocyte stimulating factor, or parathyroid hormone. (All claimed).

ADVANTAGE - The method improves the clinical use of **intra**dermal delivery of drugs, diagnostic agents, and other substances to humans or animals. The placement of the dermal access mechanism, i.e. the outlet, within the dermis provides for efficacious delivery and pharmacokinetic control of active substances by preventing leakage of the substance

from the skin and improving adsorption within the **intradermal** space. The invention achieves more rapid systemic distribution and offset, higher bioavailabilities, and higher maximum concentrations of drugs or diagnostic agents, and provides no change in systemic elimination rates or intrinsic clearance mechanisms of drugs or diagnostic agents, and in pharmacodynamic mechanism or biological response mechanism. It also provides highly controllable dosing regimens and reduced degradation of drugs and diagnostic agents and/or undesirable immunogenic activity.

pp; 47 DwgNo 0/7

International Patent Class (Main): A61M-037/00
International Patent Class (Additional): A61M-005/30; A61M-005/32

8/3,AB,IC/12 (Item 12 from file: 350)

DIALOG(R)File 350:Derwent WPIX
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014327281
WPI Acc No: 2002-147984/200219
Related WPI Acc No: 2001-275185; 2002-147985; 2002-188692; 2002-656032; 2003-046890; 2003-058613; 2003-092966; 2003-689556; 2003-810631
XRAM Acc No: C02-045977
XRPX Acc No: N02-112151

Needle for intradermal delivery of substance into human or animal skin comprises hub to limit penetration of the needle into the skin, and outlet so positioned to prevent leakage of the substance to the skin surface

Patent Assignee: BECTON DICKINSON & CO (BECT)
Inventor: **DOWN J A** ; NOEL H G; **PETTIS R J** ; HARVEY N G
Number of Countries: 097 Number of Patents: 008
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200202178	A1	20020110	WO 2001US20763	A	20010629	200219	B
AU 200175853	A	20020114	AU 200175853	A	20010629	200237	
EP 1296742	A1	20030402	EP 2001953399	A	20010629	200325	
			WO 2001US20763	A	20010629		
BR 200112314	A	20030624	BR 200112314	A	20010629	200343	
			WO 2001US20763	A	20010629		
KR 2003017567	A	20030303	KR 2002717786	A	20021227	200345	
KR 2003019464	A	20030306	KR 2002717785	A	20021227	200345	
CN 1454104	A	20031105	CN 2001811882	A	20010629	200408	
JP 2004501724	W	20040122	WO 2001US20763	A	20010629	200411	
			JP 2002506799	A	20010629		

Priority Applications (No Type Date): US 2000606909 A 20000629
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200202178	A1	E	23	A61M-037/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200175853	A		A61M-037/00	Based on patent WO 200202178
EP 1296742	A1	E	A61M-037/00	Based on patent WO 200202178

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

BR 200112314	A		A61M-037/00	Based on patent WO 200202178
KR 2003017567	A		A61M-037/00	

KR 2003019464 A A61M-037/00
CN 1454104 A A61M-037/00
JP 2004501724 W 34 A61M-037/00 Based on patent WO 200202178
Abstract (Basic): WO 200202178 A1
Abstract (Basic):

NOVELTY - Needle comprises hub for limiting penetration of the needle into the skin, and an outlet such that when the needle is inserted into the skin to a depth determined by the penetration limiting mechanism, leakage of the substance to the surface of the skin is prevented.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for delivering a substance into skin, which comprises delivering the substance into an **intradermal** space within the skin through a small gauge needle inserted into the **intradermal** space.

USE - The needle is used for **intradermal** delivery of a substance into a human or animal skin. The substance is a liquid delivered by pressure directly on the liquid, preferably a hormone including insulin and parathyroid hormone (PTH). It can be infused or injected as a bolus. The needle can be microneedles, catheter needles, or injection needles. (All claimed)

ADVANTAGE - The invention improves the clinical utility of **intradermal** (ID) delivery of drugs and other substances to humans or animals. ID infusion reduces the amount of substance lost to the skin surface and minimizes effusion of the substance out of the tissue. It also reduces painful swelling, tissue distension, and internal pressure. Placing the needle outlet at an appropriate depth in the **intradermal** space and the control of the volume and rate of fluid delivery provide accurate delivery of the substance to the desired location without leakage.

pp; 23 DwgNo 0/5

International Patent Class (Main): A61M-037/00
International Patent Class (Additional): A61K-038/22; A61K-038/28; A61P-003/10

8/3,AB,IC/13 (Item 13 from file: 350)

DIALOG(R)File 350:Derwent WPIX

014293562
WPI Acc No: 2002-114264/200215
XRAM Acc No: C02-035019
XRPX Acc No: N02-085226

Delivering a substance e.g. nucleic acid-based vaccines and peptides or polypeptides into the skin involves simultaneously abrading the skin and delivering the substance

Patent Assignee: BECTON DICKINSON & CO (BECT); ALARCON J (ALAR-I); BRITTINGHAM J M (BRIT-I); DEKKER J P (DEKK-I); MIKSZTA J A (MIKS-I); PETTIS R J (PETT-I)
Inventor: ALARCON J; BRITTINGHAM J M; DEKKER J P; MIKSZTA J A; **PETTIS R J**
Number of Countries: 095 Number of Patents: 008
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200189622	A1	20011129	WO 2001US16121	A	20010518	200215 B
AU 200161757	A	20011203	AU 200161757	A	20010518	200221
EP 1289599	A1	20030312	EP 2001935686	A	20010518	200320
			WO 2001US16121	A	20010518	
US 6595947	B1	20030722	US 2000576643	A	20000522	200354

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CN 1430526      A    20030716  CN 2001809915    A    20010518  200363
US 20030191085  A1   20031009  US 2000576643    A    20000522  200367
                                 US 2003436757    A    20030513
JP 2003534065   W    20031118  JP 2001585860    A    20010518  200401
                                 WO 2001US16121   A    20010518
BR 200111345    A    20040203  BR 200111345     A    20010518  200413
                                 WO 2001US16121   A    20010518
Priority Applications (No Type Date): US 2000576643 A 20000522; US
  2003436757 A 20030513
Patent Details:
Patent No  Kind Lan Pg   Main IPC     Filing Notes
WO 200189622  A1 E  20 A61M-035/00
   Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
   CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
   KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT
   RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
   Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
   IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
AU 200161757  A         A61M-035/00   Based on patent WO 200189622
EP 1289599    A1 E      A61M-035/00   Based on patent WO 200189622
   Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT
   LI LT LU LV MC MK NL PT RO SE SI TR
US 6595947    B1        A61M-001/00
CN 1430526    A         A61M-035/00
US 20030191085 A1        A61K-048/00   Cont of application US 2000576643
                                       Cont of patent US 6595947
JP 2003534065 W      22 A61M-037/00   Based on patent WO 200189622
BR 200111345  A         A61M-035/00   Based on patent WO 200189622
Abstract (Basic): WO 200189622 A1
Abstract (Basic):
        NOVELTY - Delivering a substance into the skin involves
    simultaneously abrading the skin and delivering the substance into the
    skin.
        DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a
    device for delivering the substance into the skin comprising:
        (i) an abrading surface coated with the substance and
        (ii) a reservoir containing a reconstituting liquid in fluid
    communication with the abrading surface.
        USE - For delivering a substance such as a nucleic acid, amino
    acid, amino acid derivative, peptide or polypeptide to the skin
    (claimed).
        ADVANTAGE - The method is more efficient and efficacious and
    results in improved delivery and response of the substance compared to
    the delivery by post-abrasion application. The nucleic acids exhibit
    enhanced gene expression and enhanced immune response to the expressed
    protein, with a minimal abrasion (as little as one pass over the skin).
    The nucleic acid delivery is also possible even without the enhancers
    and is more efficient when compared to the intramuscular (IM) delivery.
    The allergens produce a more vigorous immune response than produced
    with the conventional allergen testing methods. This produces a more
    sensitive test and has the advantage that a minor or imperceptible
    response to the conventional allergen test may be more easily detected
    using the present invention. The amount of the delivery and expression
    continues to increase with the increasing numbers of abrasive passes.
        pp; 20 DwgNo 0/4
International Patent Class (Main): A61K-048/00; A61M-001/00; A61M-035/00;
```

A61M-037/00
International Patent Class (Additional): A61B-017/20

8/3,AB,IC/14 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00995516
Transdermal patches and methods for inactivating skin proteases
Transdermale Pflaster und Verfahren zur Inaktivierung von Hautproteasen
Emplatres transdermiques et methodes d'inactivation de proteases de la peau
PATENT ASSIGNEE:
Becton, Dickinson and Company, (208883), One Becton Drive, Franklin Lakes, New Jersey 07417-1880, (US), (applicant designated states: AT;BE;CH;CY;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Down, James Arthur , 814 Oakley Court, Cary, NC 27511, (US)
Williams, Amy Casey, 13321 Ludlow Avenue, Huntington Woods, MI 48070, (US
LEGAL REPRESENTATIVE:
Ruffles, Graham Keith (43041), MARKS & CLERK, 57-60 Lincoln's Inn Fields, London WC2A 3LS, (GB)
PATENT (CC, No, Kind, Date): EP 898962 A1 990303 (Basic)
APPLICATION (CC, No, Date): EP 98306942 980828;
PRIORITY (CC, No, Date): US 919829 970828
DESIGNATED STATES: DE; FR; GB
INTERNATIONAL PATENT CLASS: A61K-009/70; A61K-038/04; A61K-047/00; A61K-047/02; A61K-047/04; A61N-001/20; A61N-001/30;
ABSTRACT EP 898962 A1
Methods of inactivating skin proteases in order to permit the transdermal delivery of peptide drugs, specifically via iontophoretic patches, are described. In general, the methods involve inhibiting one or more proteases in a patient's stratum corneum by using an agent which reacts with histidine residues within the proteases. Specific examples of such methods include use of compounds which are specifically reactive with histidine residues in proteins; use of iodine containing compounds; use of hydrogen peroxide; use of indole reactive compounds; use of ultra-violet light; use of disulfide reducing reagents; controlling pH; use of zinc in conjunction with high pH; and use of oxidizing compounds. Transdermal patches including agents which react with histidine residues in skin proteases are also described.
ABSTRACT WORD COUNT: 120
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9909	196
SPEC A	(English)	9909	6281
Total word count - document A			6477
Total word count - document B			0
Total word count - documents A + B			6477

8/3,AB,IC/15 (Item 15 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

01036430
DEVICE AND METHOD FOR DELIVERING OR WITHDRAWING A SUBSTANCE THROUGH THE SKIN
DISPOSITIF ET PROCEDE D'ADMINISTRATION OU D'EXTRACTION D'UNE SUBSTANCE PAR

VOIE CUTANEE

Patent Applicant/Assignee:
BECTON DICKINSON AND COMPANY, Intellectual Property Department, Mail Code 089, 1 Becton Drive, Franklin Lakes, NJ 07417-1880, US, US (Residence), US (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:
LASTOVICH Alexander G, 8800 Klondike Court, Raleigh, NC 27615, US, US (Residence), US (Nationality), (Designated only for: US)
FENTRESS Jim K, 2309 Duck Pond Circle, Apt.1, Morrisville, NC 27560, US, US (Residence), US (Nationality), (Designated only for: US)
GRIGGS Julia E, 500C Golden Horseshoe Circle, Morrisville, NC 27560, US, US (Residence), US (Nationality), (Designated only for: US)
PETTIS Ronald J , 529 Darby Glen Lane, Durham, NC 227713, US, US (Residence), US (Nationality), (Designated only for: US)
SUTTER Diane E, 107 N. Atley Lane, Cary, NC 27513, US, US (Residence), US (Nationality), (Designated only for: US)
MARTIN Frank E, 2807 Barton Road, Durham, NC 27717-1595, US, US (Residence), US (Nationality), (Designated only for: US)
HAIDER M Ishaq, 204 Ketrick Court, Morrisville, NC 27560, US, US (Residence), US (Nationality), (Designated only for: US)
LOCKHART Artis R, 803 Corona Street, Durham, NC 27707, US, US (Residence), US (Nationality), (Designated only for: US)
POWELL Kenneth G, 4513 Wood Valley Drive, Raleigh, NC 27613, US, US (Residence), US (Nationality), (Designated only for: US

Legal Representative:
SCHMIDT Richard D (agent), Venable, Baetjer, Howard & Civiletti, LLP, 1201 New York Avenue, Suite 1000, P.O. Box 34385, Washington, DC 20043-9998, US,

Patent and Priority Information (Country, Number, Date):
Patent: WO 200366126 A2 20030814 (WO 0366126)
Application: WO 2003US3424 20030204 (PCT/WO US0303424)
Priority Application: US 2002353194 20020204; US 2002377649 20020506; US 2002389881 20020620; US 2002397038 20020722; US 2002407284 20020903; US 2002420233 20021023

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: A61M
Publication Language: English
Filing Language: English
Fulltext Word Count: 10388

English Abstract

An apparatus for delivering or withdrawing a fluid through at least one layer of the skin is provided. A device includes a body having a top face, a bottom face, a side edge and at least one channel. The bottom face includes a first surface area and a second surface area adjacent to and recessed at a first distance from the first surface area. The bottom face further includes at least one raised protrusion disposed on the second surface area. The protrusion has a height from the first surface greater than the first distance. At least one dermal-access member is provided in the protrusion and is in fluid communication with the channel

to deliver or withdraw the fluid. The dermal-access member extends at least 1 mm from the protrusion. A mechanism drives the device against the skin at a calculated speed of about 6 m/s to about 18 m/s.

8/3,AB,IC/16 (Item 16 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

01021679
METHOD AND DEVICE FOR THE DELIVERY OF A SUBSTANCE
PROCEDE ET DISPOSITIF D'ADMINISTRATION D'UNE SUBSTANCE
Patent Applicant/Assignee:
BECTON DICKINSON AND COMPANY, Intellectual Property Department, Mail Code 089, 1 Becton Drive, Franklin Lakes, NJ 07417-1880, US, US (Residence), US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
MIKSZTA John A, 115 Wood Valley Ct., Durham, NC 27713, US, US (Residence), US (Nationality), (Designated only for: US)
PETTIS Ronald J , 101 Langdale Place, Cary, NC 27513, US, US (Residence), US (Nationality), (Designated only for: US)
ALARCON Jason, 230 Newberry Lane, Durham, NC 27703, US, US (Residence), AU (Nationality), (Designated only for: US)
BRITTINGHAM John M, 3113 Billiard Court, Wake Forest, NC 27587, US, US (Residence), US (Nationality), (Designated only for: US)
DEKKER III John P, 504 Edgemore Avenue, Cary, NC 27516, US, US (Residence), US (Nationality), (Designated only for: US
Legal Representative:
HOBBS Ann S (agent), Venable, Baetjer, Howard & Civiletti, LLP, 1201 New York Avenue, Suite 1000, P.O. Box 34385, Washington, DC 20043-9998, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200351284 A2-A3 20030626 (WO 0351284)
Application: WO 2002US34504 20021029 (PCT/WO US02034504)
Priority Application: US 2001330713 20011029; US 2001333162 20011127
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class: A61M-001/00
Publication Language: English
Filing Language: English
Fulltext Word Count: 16649
English Abstract
An abrasion device and method for delivery of substances into the skin comprises a microabrader (2) for delivering a substance into the skin having a base (14) with an abrading facet, to which an abrading surface (5) having an arrangement of microprotrusions that have at least one scraping edge is attached, mounted, or integral with and a handle attachment facet, to which a handle (6) or other grasping device is attached or mounted.

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File 155:MEDLINE(R) 1966-2004/May W5
File   5:Biosis Previews(R) 1969-2004/May W5
File  73:EMBASE 1974-2004/May W5
File  34:SciSearch(R) Cited Ref Sci 1990-2004/May W5
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
Set     Items   Description
S1         32   AU='PETTIS R' OR AU='PETTIS R J' OR AU='PETTIS R.' OR AU='-
              PETTIS R.J.' OR AU='PETTIS RJ' OR AU='PETTIS RONALD J'
S2        142   AU='DOWN J' OR AU='DOWN J A' OR AU='DOWN J.' OR AU='DOWN J-
              .A.' OR AU='DOWN JA' OR AU='DOWN JAMES' OR AU='DOWN JAMES A'
S3        195   AU='HARVEY N' OR AU='HARVEY N G' OR AU='HARVEY N.' OR AU='-
              HARVEY N.G.' OR AU='HARVEY NG' OR AU='HARVEY NOEL G'
S4          0   S1 AND S2 AND S3
S5      39142   INTRADERMAL?
S6          1   S1:S3 AND S5
S7        702   MICRONEEDLE?
S8          2   S1:S3 AND S7
S9          2   S8 NOT S6
S10         2   RD (unique items)

 6/9/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2004 Elsevier Science B.V. All rts. reserv.
11574466     EMBASE No: 2002145006
  Improved genetic immunization via micromechanical disruption of
skin-barrier function and targeted epidermal delivery
  Mikszta J.A.; Alarcon J.B.; Brittingham J.M.; Sutter D.E.; Pettis R.J. ;
 Harvey N.G.
  J.A. Mikszta, BD Technologies, Research Triangle Park, NC  United States
  AUTHOR EMAIL: john mikszta@bd.com
  Nature Medicine ( NAT. MED. ) (United States)   2002, 8/4 (415-419)
  CODEN: NAMEF   ISSN: 1078-8956
  DOCUMENT TYPE: Journal ; Article
  LANGUAGE: ENGLISH   SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 20
  Skin is an attractive target for delivery of genetic therapies and
vaccines. However, new approaches are needed to access this tissue more
effectively. Here, we describe a new delivery technology based on arrays of
structurally precise, micron-scale silicon projections, which we term
microenhancer arrays (MEAs). In a human clinical study, these devices
effectively breached the skin barrier, allowing direct access to the
epidermis with minimal associated discomfort and skin irritation. In a
mouse model, MEA-based delivery enabled topical gene transfer resulting in
reporter gene activity up to 2,800-fold above topical controls. MEA-based
delivery enabled topical immunization with naked plasmid DNA, inducing
stronger and less variable immune responses than via needle-based
injections, and reduced the number of immunizations required for full
seroconversion. Together, the results provide the first in vivo use of
microfabricated devices to breach the skin barrier and deliver vaccines
topically, suggesting significant clinical and practical advantages over
existing technologies.
DRUG DESCRIPTORS:
vaccine; plasmid DNA-- intradermal  drug administration--dl; plasmid DNA
--intramuscular drug administration--im; silicon
MEDICAL DESCRIPTORS:
*immunization; *epidermis; *gene targeting
```

gene disruption; gene therapy; genetic procedures; skin irritation; reporter gene; immune response; device; gene expression; skin protection; accuracy; genetic engineering; gene delivery system; nonhuman; female; mouse; animal experiment; animal model; controlled study; animal tissue; article; priority journal
MEDICAL TERMS (UNCONTROLLED): microenhancer array
CAS REGISTRY NO.: 7440-21-3 (silicon)
SECTION HEADINGS:
022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index

10/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014762386 BIOSIS NO.: 200400143143
Microdevice and method of delivering or withdrawing a substance through the skin of an animal
AUTHOR: Connelly Robert I (Reprint); **Pettis Ronald J**
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1279 (2): Feb. 10, 2004 2004
MEDIUM: e-file
PATENT NUMBER: US 6689100 PATENT DATE GRANTED: February 10, 2004 20040210
PATENT CLASSIFICATION: 604-117 PATENT ASSIGNEE: Becton, Dickinson and Company PATENT COUNTRY: USA
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: A device for withdrawing or delivering a substance through the skin of a patient includes a body and a skin penetrating device having a plurality of skin penetrating members, such **microneedles** . The body includes a bottom surface having a first inner surface area supporting the skin penetrating members and a second outer surface having an adhesive for attaching the device to the skin. In one embodiment, the firs inner surface is spaced outwardly from the second outer surface when the device is attached to the skin. The inner surface can have a textured visually wettable surface, such as an etched surface, to provide a visual indication of leakage from the interface between the skin penetrating members and the skin.
DESCRIPTORS:
MAJOR CONCEPTS: Equipment Apparatus Devices and Instrumentation; Human Medicine--Medical Sciences
METHODS & EQUIPMENT: body and skin penetrating device--medical equipment; microdevice--medical equipment; **microneedles** --medical equipment
CONCEPT CODES:
12502 Pathology - General

10/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014677905 BIOSIS NO.: 200400058662
Method and delivery device for the transdermal administration of a substance
AUTHOR: Gertsek Marina (Reprint); Wilkinson Bradley M; **Pettis Ronald J**
AUTHOR ADDRESS: Ridgewood, NJ, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office

Patents 1277 (1): Dec. 2, 2003 2003
MEDIUM: e-file
PATENT NUMBER: US 6656147 PATENT DATE GRANTED: December 02, 2003 20031202
PATENT CLASSIFICATION: 604-28 PATENT ASSIGNEE: Becton, Dickinson and Company PATENT COUNTRY: USA
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: A device for delivering a substance into the skin of a patient includes a housing and a plurality of **microneedles** for penetrating the skin. The housing includes a bottom wall with a plurality of apertures for supplying the substance to the **microneedles** . The housing also includes a flexible top cover member enclosing a bladder containing the substance to be delivered. The bottom wall of the housing has at least one cannula facing the bladder. Pressing on the top cover member causes the cannula to puncture the bladder and deliver the substance to the **microneedles** for delivery to the patient. In one embodiment, the cannula is surrounded by a flexible member to prevent piercing of the bladder until sufficient pressure is applied to the cover member to depress the flexible member.
DESCRIPTORS:
MAJOR CONCEPTS: Equipment Apparatus Devices and Instrumentation; Methods and Techniques; Pharmacy--Allied Medical Sciences
METHODS & EQUIPMENT: transdermal substance administration delivery device --drug delivery device; transdermal substance administration delivery method--clinical techniques, therapeutic and prophylactic techniques
CONCEPT CODES:
12512 Pathology - Therapy
22002 Pharmacology - General

File 155:MEDLINE(R) 1966-2004/May W5

Set	Items	Description
S1	15219	'INJECTIONS, INTRADERMAL' OR 'MICROINJECTIONS'
S2	61834	NEEDLE? ? OR MICRONEEDLE? ?
S3	175	S1 AND S2
S4	8197	OUTLET
S5	0	S3 AND S4
S6	39313	UM OR MICRON OR MICRONS
S7	268080	MM OR MILLIMETER? ? OR MILLIMETRE? ?
S8	**2**	**S3 AND S6**
S9	**12**	**S3 AND S7**
S10	0	S8 AND S9
S11	190756	INSULIN OR PTH
S12	2	S3 AND S11
S13	**2**	**S12 NOT S8:S9**

8/6/2

12975581 PMID: 8636465

Migration of A7 immortalized astrocytic cells grafted into the adult rat striatum.

Nov 27 1995

8/9/1

DIALOG(R)File 155:MEDLINE(R)

13989311 PMID: 9687334

Microfabricated microneedles **: a novel approach to transdermal drug delivery.**

Henry S; McAllister D V; Allen M G; Prausnitz M R

Institute for Bioengineering and Bioscience, School of Chemical Engineering, Georgia Institute of Technology, Atlanta, Georgia 30332, USA.

Journal of pharmaceutical sciences (UNITED STATES) Aug 1998, 87 (8) p922-5, ISSN 0022-3549 Journal Code: 2985195R

Erratum in J Pharm Sci 1998 Sep;88(9) 948

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Although modern biotechnology has produced extremely sophisticated and potent drugs, many of these compounds cannot be effectively delivered using current drug delivery techniques (e.g., pills and injections). Transdermal delivery is an attractive alternative, but it is limited by the extremely low permeability of skin. Because the primary barrier to transport is located in the upper 10-15 **micron** of skin and nerves are found only in deeper tissue, we used a reactive ion etching microfabrication technique to make arrays of **microneedles** long enough to cross the permeability barrier but not so long that they stimulate nerves, thereby potentially causing no pain. These **microneedle** arrays could be easily inserted into skin without breaking and were shown to increase permeability of human skin in vitro to a model drug, calcein, by up to 4 orders of magnitude. Limited tests on human subjects indicated that **microneedles** were reported as painless. This paper describes the first published study on the use of microfabricated **microneedles** to enhance drug delivery across skin.

Tags: Human; In Vitro; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Administration, Cutaneous; * **Needles** ; Fluoresceins --administration and dosage--AD; Fluoresceins--pharmacokinetics--PK; Fluorescent Dyes--administration and dosage--AD; Fluorescent Dyes --pharmacokinetics--PK; **Microinjections** --instrumentation--IS; **Microinjections** --methods--MT; Microscopy, Electron, Scanning
CAS Registry No.: 0 (Fluoresceins); 0 (Fluorescent Dyes); 1461-15-0 (fluorexon)
Record Date Created: 19980903
Record Date Completed: 19980903

9/6/2
13628047 PMID: 9314529
Large plasma membrane disruptions are rapidly resealed by Ca2+-dependent vesicle-vesicle fusion events.
Oct 6 1997

9/6/3
13118373 PMID: 8784280
Eutectic lidocaine/prilocaine 5% cream and patch may provide satisfactory analgesia for excisional biopsy or curettage with electrosurgery of cutaneous lesions. A randomized, controlled, parallel group study.
Sep 1996

9/6/4
12946509 PMID: 8612859
The hypo-osmotic swelling test for selection of viable sperm for intracytoplasmic sperm injection in men with complete asthenozoospermia.
May 1996

9/6/5
12771928 PMID: 7573921
EMLA cream prior to insertion of elective epidurals.
Jun 1995

9/6/6
12428265 PMID: 12832888
Investigation of the growth and metastasis of malignant melanoma in a murine model: the role of supplemental vitamin A.
Jul 2003

9/6/10
06596790 PMID: 6470781
Intracranial pressure variations associated with activation of the cholinoceptive pontine inhibitory area in the unanesthetized drug-free cat.
Oct 1984

9/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
13818028 PMID: 9517682
Effect of temperature and pH adjustment of bupivacaine for intradermal anesthesia.
Jones J S; Plzak C; Wynn B N; Martin S
Department of Emergency Medicine, Butterworth Hospital, Grand Rapids, MI, USA.
American journal of emergency medicine (UNITED STATES) Mar 1998, 16

(2) p117-20, ISSN 0735-6757 Journal Code: 8309942
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

To determine the effects of warming and buffering of 0.5% bupivacaine on the pain associated with **intradermal injection** and the time of onset of anesthesia, 40 adult volunteers were entered into a randomized, double-blind study conducted at a community teaching hospital. The three-part study compared room temperature (20 degrees) bupivacaine buffered to a pH of 7.1 with the following solutions: buffered bupivacaine warmed to 37 degrees C, unbuffered bupivacaine at room temperature, and unbuffered bupivacaine warmed to 37 degrees C. The same crossover protocol was followed for each part of the study. Subjects received 0.5-mL intradermal injections through 27-gauge **needles** over 30 seconds, one study solution in each forearm. Immediately after each injection, pain was assessed using a 100- **mm** visual analog pain scale. The time of onset of anesthesia (loss of intradermal sensation to pinprick) was measured by stopwatch. The mean perceived pain score for the warm buffered bupivacaine (51 **mm**) was significantly lower than for the room temperature buffered solution (63 **mm** , P = .003). Similarly, there was a statistical difference between the room temperature buffered and unbuffered solutions (65 v 78 **mm** , P < .001). The differences in mean pain scores for the room temperature buffered bupivacaine, compared with the other three solutions, suggest that warming and buffering have an additive effect. In this model, the latency of action of bupivacaine was not affected by alkalinization. However, warming bupivacaine to 37 degrees C reduced the time of onset to intradermal anesthesia by 12.1 seconds (95% confidence interval, 0.6 to 23.6). These results suggest that warming is more effective than buffering to reduce the pain of infiltration of bupivacaine and the time of onset of intradermal anesthesia.

Tags: Comparative Study; Human
Descriptors: *Anesthesia, Local; *Anesthetics, Local--administration and dosage--AD; *Bupivacaine--administration and dosage--AD; Adult; Alkalies --chemistry--CH; Anesthetics, Local--chemistry--CH; Buffers; Bupivacaine --chemistry--CH; Confidence Intervals; Cross-Over Studies; Double-Blind Method; Forearm; Heat; Hospitals, Community; Hospitals, Teaching; Hydrogen-Ion Concentration; **Injections, Intradermal** --adverse effects--AE; Pain--etiology--ET; Pain Measurement; Sensation--drug effects--DE; Temperature; Time Factors
CAS Registry No.: 0 (Alkalies); 0 (Anesthetics, Local); 0 (Buffers) ; 2180-92-9 (Bupivacaine)
Record Date Created: 19980407
Record Date Completed: 19980407

9/9/7
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
10060469 PMID: 8172738

Percutaneous ethanol injection therapy of adenomatous hyperplastic nodules in cirrhotic liver disease.

Lencioni R; Caramella D; Bartolozzi C; Mazzeo S; Di Coscio G
Department of Radiology, University of Pisa, Italy.
Acta radiologica (Stockholm, Sweden - 1987) (DENMARK) Mar 1994, 35

(2) p138-42, ISSN 0284-1851 Journal Code: 8706123
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Adenomatous hyperplastic nodules (AHNs) in cirrhotic liver are considered a precancerous condition which may lead to hepatocellular carcinoma (HCC). In this study, we treated a total of 23 AHNs in 15 patients with percutaneous ethanol injection (PEI). The treatment included 6 to 8 PEIs, performed on an out-patient basis under sonographic guidance. A 22 G (0.7 **mm**) spinal **needle** was used. The total amount of alcohol delivered into each lesion was 8 to 25 ml (mean 14.9 ml). At the end of treatment, complete necrosis of the nodule was proved in all cases by multiple fine-**needle** biopsies and confirmed by CT and MR findings. During follow-up (9-41 months, mean 24 months) no recurrences were demonstrated. However, HCC occurred elsewhere in the liver of 4 patients and additional AHNs were detected in 2 patients. Thus, PEI proved able to cause complete ablation of AHNs, presumably preventing their malignant transformation. However, patients with AHN remain at high risk for developing HCC.

Tags: Female; Human; Male
Descriptors: *Ethanol--therapeutic use--TU; *Liver Cirrhosis --complications--CO; *Liver Neoplasms--drug therapy--DT; *Precancerous Conditions--drug therapy--DT; Aged; Carcinoma, Hepatocellular--pathology --PA; Ethanol--administration and dosage--AD; Hyperplasia; **Injections, Intradermal** ; Liver Cirrhosis--diagnosis--DI; Liver Cirrhosis--pathology --PA; Middle Aged
CAS Registry No.: 64-17-5 (Ethanol)
Record Date Created: 19940606
Record Date Completed: 19940606

9/9/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
08720296 PMID: 2245318

Further studies of the effects of intranigral morphine on behavioral responses to noxious stimuli.

Baumeister A A; Nagy M; Hebert G; Hawkins M F; Vaughn A; Chatellier M O
Department of Psychology, Louisiana State University, Baton Rouge 70803.
Brain research (NETHERLANDS) Aug 13 1990, 525 (1) p115-25, ISSN 0006-8993 Journal Code: 0045503
Contract/Grant No.: DA05907; DA; NIDA
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Bilateral intranigral **microinjection** of morphine produces dose-related and naloxone reversible analgesic-like effects on the hot-plate and tail-flick tests. The main objectives of the present studies were to further characterize the analgesic-like effects of intranigral morphine, to determine whether these effects were related to a general impairment of sensory or motor function, and to assess their anatomical specificity. The principal findings are: (1) intranigral morphine (10 micrograms) suppresses pain-related behavior without altering responses to a variety of non-noxious auditory, visual, and somatic stimuli, and without producing

motor impairment; (2) movement of injector **needles** approximately 1 **mm** rostral, dorsal, or medial to the active nigral site significantly reduces the analgesic-like effect of morphine on the tail-flick test; and (3) electrolytic lesions confined to the nigra significantly reduced the analgesic-like effect of morphine on the hot-plate test. It is concluded that the analgesic-like effects of intranigral morphine are mediated by the substantia nigra and that these effects are specifically related to pain.

Tags: Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Morphine--pharmacology--PD; *Pain--physiopathology--PP; *Psychomotor Performance--drug effects--DE; *Substantia Nigra--drug effects --DE; *Substantia Nigra--physiology--PH; Animals; Formaldehyde; Mesencephalon--drug effects--DE; **Microinjections** ; Periaqueductal Gray --drug effects--DE; Rats; Rats, Inbred Strains; Reticular Formation--drug effects--DE; Substantia Nigra--pathology--PA; Tegmentum Mesencephali--drug effects--DE

CAS Registry No.: 50-00-0 (Formaldehyde); 57-27-2 (Morphine)

Record Date Created: 19910108

Record Date Completed: 19910108

9/9/9

DIALOG(R)File 155:MEDLINE(R)

07968598 PMID: 3144335 Record Identifier: 051977; 00182580

BCG immunisation of infants by percutaneous multiple puncture.

Cundall D B; Ashelford D J; Pearson S B

Department of Paediatrics and Child Health, St James's University Hospital, Leeds.

BMJ (Clinical research ed.) (ENGLAND) Nov 5 1988, 297 (6657) p1173-4 , ISSN 0959-8138 Journal Code: 8900488

TJ: BMJ : BRITISH MEDICAL ASSOCIATION.

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Other Citation Owner: PIP; POP

Abstract Source: PIP

Record type: Completed

Subfile: AIM; INDEX MEDICUS

The safety, efficacy, and ease of administration of percutaneous multiple-puncture gun immunization of infants with BCG was compared with **intradermal injection** with a syringe. 214 consecutive infants scheduled for BCG were alternately given percutaneous or **intradermal injections** over the left deltoid muscle by 1 of 3 doctors. The Modified Heaf gun with 20 **needles set to penetrate 1 mm** , or a syringe with a 24 gauge short beveled **needle** was used. Doctors recorded bleeding and ease of administering the vaccine. The intradermal method was recorded as difficult in 36 cases, very difficult in 4, and the percutaneous method was deemed difficult in 1 case. Of the 200 infants remaining in contact 3-7 days later, 141 were read as positive. There were no significant differences in amount of bleeding or seroconversion. A difference in seroconversion was observed, however, between the different doctors using the intradermal technique. The percutaneous method resulted in less ulceration and scarring, gave consistent seroconversion, and was easier to administer.

Tags: Comparative Study; Female; Human; Male

Descriptors: *BCG Vaccine--administration and dosage--AD; Administration, Cutaneous; Infant; **Injections, Intradermal** ; Tuberculosis--prevention and control--PC

CAS Registry No.: 0 (BCG Vaccine)
Identifiers: *Age Factors; *Antibodies; *Antibody Formation; *Bacterial And Fungal Diseases; *Biology; *Clinical Research; *Delivery Of Health Care ; *Demographic Factors; *Developed Countries; *Diseases; *Economic Factors; *England; *Equipment And Supplies; *Europe; *Health; *Health Services; *Human Volunteers; *Immunity; *Immunity, Cellular; *Immunization; *Immunologic Factors; *Infant; *Infections; *Medicine; *Northern Europe; *Physiology; *Population; *Population Characteristics; *Preventive Medicine ; *Primary Health Care; *Research And Development; *Research Methodology; *Syringe; *Technology; *Tuberculosis; *United Kingdom; *Vaccination; *Youth
Record Date Created: 19890207
Record Date Completed: 19890207

9/9/11
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
04235272 PMID: 1259468
Effect of needle **puncture and intradermal fluid injection on epidermal cell kinetics of albino guinea-pig skin.**
Taguchi Y H; Tabachnick J; Manaka K
Archives for dermatological research. Archiv fur dermatologische Forschung (GERMANY, WEST) Mar 10 1976, 255 (1) p83-92, ISSN 0340-3696 Journal Code: 7512589
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The flanks of male albino guinea pigs were used to study the effect of **needle** puncture with or without **intradermal (id) injection** of 0.1 ml fluid. The center of the raised bleb was marked and biopsies taken 1,4,8,24,50 and 72 hrs after **needle** puncture and 1 hr after intraperitoneal (ip) injection of tritiated thymidine (3H-TdR). There were no significant differences in labeling index (LI) or mitotic index (MI) 1 hr after id, ip, or subcutaneous (sc) injection nor in percent labeled mitoses, 7 hrs after id or ip injection. The earliest increase in LI (180% above control) occurred 12 hrs after **needle** puncture, peaked at 24 hrs (ca. 3X control), and returned to control level by 50 hrs. The area affected had a radius of about 5 **mm** from the point of **needle** entry or center of the bleb. Within 12 hrs after **needle** puncture, there was an increase in labeled cells primarily at the periphery of the bleb area, about 4 **mm** from the point of **needle** entry. By 24 hrs, the distribution of labeled cells had moved toward the bleb center (LI = 65%). The first increase in mitoses (MI = 2.5%) was seen 24 hrs after **needle** puncture. It is concluded that id injection introduces no significant error in LI or MI to 8 hrs after **needle** puncture. It does, however, trigger many noncycling basal cells into DNA synthesis after 8 hrs, and this may increase the rate of transit of these cells to the granular layer.
Tags: Male
Descriptors: *Cell Movement; *Punctures; *Skin--injuries--IN; Animals; Autoradiography--methods--MT; DNA--biosynthesis--BI; **Injections, Intraderm al** ; Mitotic Index; Radioisotopes--administration and dosage--AD; Skin --cytology--CY
CAS Registry No.: 0 (Radioisotopes); 9007-49-2 (DNA)
Record Date Created: 19760520
Record Date Completed: 19760520

9/9/12
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
04136332 PMID: 1181681
A study to assess the intradermal, triangular needle **and bifurcated** needle **techniques in the administration of BCG to newborns.**
Allan W G
Tubercle (SCOTLAND) Jun 1975, 56 (2) p139-47, ISSN 0041-3879 Journal Code: 1273730
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
BCG at birth was administered to 3,297 new born babies in Hong Kong using the **intradermal**, simple triangular and bifurcated **needle** techniques. Tuberculin testing at 3 months showed similar mean reactions for the intradermal and simple triangular **needle** methods, namely 9-74 **mm** and 9-87 **mm** with 9-94 **mm** for the triangular **needle** method when the BCG strength was doubled. Using the bifurcated **needle** the mean reactions were significantly lower; 8-69 **mm** , 9-01 **mm** with double strength BCG and 8-92 **mm** with puncture through a skin drop. It is concluded that the bifurcated **needle** is not a satisfactory method of administering BCG to newborns even if the concentration of BCG is increased. In circumstances such as in small maternity units, where the intradermal technique is not warranted, it is recommended that the simple triangular method should be used.
Tags: Comparative Study; Human
Descriptors: *BCG Vaccine--administration and dosage--AD; *Infant, Newborn; BCG Vaccine--adverse effects--AE; **Injections, Intradermal** ; **Needles** ; Tuberculin Test; Vaccination--instrumentation--IS
CAS Registry No.: 0 (BCG Vaccine)
Record Date Created: 19760108
Record Date Completed: 19760108

13/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
15556619 PMID: 14623977
Microfabricated needles **for transdermal delivery of macromolecules and nanoparticles: fabrication methods and transport studies.**
McAllister Devin V; Wang Ping M; Davis Shawn P; Park Jung-Hwan; Canatella Paul J; Allen Mark G; Prausnitz Mark R
School of Chemical and Biomolecular Engineering, Georgia Institute of Technology, Atlanta 30332, USA.
Proceedings of the National Academy of Sciences of the United States of America (United States) **Nov 25 2003**, 100 (24) p13755-60, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Arrays of micrometer-scale **needles** could be used to deliver drugs, proteins, and particles **across skin** in a minimally invasive manner. We therefore developed microfabrication techniques for silicon, metal, and

biodegradable polymer **microneedle** arrays having solid and hollow bores with tapered and beveled tips and feature sizes from **1 to 1,000 microm**. When solid **microneedles** were used, skin permeability was increased in vitro by orders of magnitude for macromolecules and particles up to 50 nm in radius. Intracellular delivery of molecules into viable cells was also achieved with high efficiency. Hollow **microneedles** permitted flow of microliter quantities into skin in vivo, including microinjection of **insulin** to reduce blood glucose levels in diabetic rats.

Tags: Human; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: **Microinjections** --instrumentation--IS; *Syringes; Administration, Cutaneous; Animals; Biomedical Engineering; Blood Glucose --metabolism--ME; Cell Line; Diabetes Mellitus, Experimental--blood--BL; Diabetes Mellitus, Experimental--drug therapy--DT; Equipment Design; Glass ; **Insulin** --administration and dosage--AD; Macromolecular Systems; Metals; Models, Biological; Nanotechnology; Polymers; Rats; Silicon

CAS Registry No.: 0 (Blood Glucose); 0 (Glass); 0 (Macromolecular Systems); 0 (Metals); 0 (Polymers); 11061-68-0 (Insulin); 7440-21-3 (Silicon)

Record Date Created: 20031203

Record Date Completed: 20040202

Date of Electronic Publication: 20031117

13/9/2

DIALOG(R)File 155:MEDLINE(R)

05313748 PMID: 6770113

Multiple use of disposable insulin **syringe-** needle **units.**

Hodge R H; Krongaard L; Sande M A; Kaiser D L

JAMA - the journal of the American Medical Association (UNITED STATES) Jul 18 1980, 244 (3) p266-7, ISSN 0098-7484 Journal Code: 7501160

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Fourteen **insulin** -dependent diabetics were asked to use their **insulin** syringe- **needle** units three times in succession to determine the efficacy and safety of this practice. The mean duration of time each patient participated in the study was 20.4 weeks, and a total of 2,000 injections were taken. No signs of infections at the injection site were observed. Multiple use of disposable **insulin** syringe- **needle** units appears to be safe and cost beneficial.

Tags: Human; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Disposable Equipment; * **Insulin** --administration and dosage --AD; * **Needles** ; *Syringes; Adult; Aged; Bacterial Infections--prevention and control--PC; Cost-Benefit Analysis; Diabetes Mellitus--drug therapy--DT ; Disposable Equipment--economics--EC; **Injections, Intradermal** ; Middle Aged; **Needles** --standards--ST; Sterilization; Syringes--standards--ST

CAS Registry No.: 11061-68-0 (Insulin)

Record Date Created: 19800828

Record Date Completed: 19800828

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File 155:MEDLINE(R) 1966-2004/May W5
File   5:Biosis Previews(R) 1969-2004/May W5
File  73:EMBASE 1974-2004/May W5
File  34:SciSearch(R) Cited Ref Sci 1990-2004/May W5
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
File 144:Pascal 1973-2004/May W4
File   6:NTIS 1964-2004/Jun W1
File   8:Ei Compendex(R) 1970-2004/May W4
File  94:JICST-EPlus 1985-2004/May W2
File  95:TEME-Technology & Management 1989-2004/May W3
File  99:Wilson Appl. Sci & Tech Abs 1983-2004/Apr
File  65:Inside Conferences 1993-2004/May W5
File  35:Dissertation Abs Online 1861-2004/May
File  71:ELSEVIER BIOBASE 1994-2004/May W4
File 357:Derwent Biotech Res. _1982-2004/Jun W1
File  42:Pharmaceuticl News Idx 1974-2004/May W4
File 285:BioBusiness(R) 1985-1998/Aug W1
File 358:Current BioTech Abs 1983-2004/May
File 583:Gale Group Globalbase(TM) 1986-2002/Dec 13
File 315:ChemEng & Biotec Abs 1970-2004/May
Set     Items   Description
S1      53915   INTRADERMAL? OR INTRA()DERMAL? OR INTRAEPIDERMAL? OR INTRA-
             ()EPIDERMAL?
S2     272017   NEEDLE? ? OR MICRONEEDLE? ?
S3     127883   OUTLET? ?
S4    2177038   MM OR MILLIMETER? ? OR MILLIMETRE? ? OR UM OR MICRON? ? OR
            MICROM? ? OR MICROMETER? ? OR MICROMETRE? ?
S5    2937371   PLASMA
S6         34   S2 AND S3 AND S4
S7       2458   (S1 OR S6) AND S5
S8    8423414   LEVEL? ?
S9   11859370   INCREAS??? OR RAISE? ? OR RAISING
S10   4783955   HIGHER
S11    374125   S5(1N)S8
S12    129105   S9(1W)S5
S13     29991   S10(2W)S5
S14       475   (S1 OR S6) AND S11:S13
S15         2   S1 AND S6
S16         0   S14 AND S15
S17         0   S15 AND  S5
S18      2266   (S1 OR S2(2N)S3) AND S4
S19        74   S5 AND S18
S20        10   S11:S13 AND S18
S21         5   RD (unique items)
S22        64   S19 NOT S20
S23        45   RD (unique items)
S24        14   S23/2001:2004
S25        31   S23 NOT S24
S26        31   Sort S25/ALL/PY,A
S27         0   S1 AND S5 AND S6
S28     16979   INTRADERMAL/DE
S29        15   S4 AND S5 AND S28
S30         0   S29 NOT S19:S20

21/7,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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13154252 PMID: 8823230
Pharmacokinetics and pharmacodynamics of the endothelin-receptor antagonist bosentan in healthy human subjects.
Weber C; Schmitt R; Birnboeck H; Hopfgartner G; van Marle S P; Peeters P A; Jonkman J H; Jones C R
Clinical and Preclinical Research and Development, F. Hoffmann-La Roche Ltd., Basel, Switzerland.
Clinical pharmacology and therapeutics (UNITED STATES) Aug 1996, 60 (2) p124-37, ISSN 0009-9236 Journal Code: 0372741
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
INTRODUCTION: Bosentan (Ro 47-0203) is a potent and mixed ETA-and ETB-receptor antagonist. Its activity has been studied in a variety of preclinical disease models. METHODS: Two double-blind placebo-controlled studies were performed to investigate the pharmacokinetics and pharmacodynamics of bosentan after single oral and intravenous doses in healthy volunteers; doses of 3, 10, 30, 100, 300, 600, 1200, and 2400 mg were given in a single ascending oral dose study, and doses of 10, 50, 250, 500, and 750 mg were given in a single ascending intravenous dose study (six subjects received active drug and two received placebo at each dose level). In an open-label crossover added to the second study, six subjects received a single oral dose of 600 mg and a single intravenous dose of 250 mg in randomized order. At regular intervals, blood pressure, pulse rate, and skin responses to **intradermally** injected endothelin-1 (ET-1) were recorded, and **plasma levels** of ET-1, proendothelin-1 (big ET-1), and ET-3, and drug and urinary levels of ET-1 and drug were determined. RESULTS: Systemic plasma clearance and volume of distribution decreased with increasing dose to limiting values of around 6 L/hr and 0.2 L/kg, respectively. The absolute bioavailability was 50% and appeared to decrease with doses above 600 mg. Plasma ET-1 increased maximally twofold (oral) and threefold (intravenous), and this increase was directly related to bosentan plasma concentrations according to an Emax model. Bosentan reversed the vasoconstrictor effect of ET-1 measured in the skin microcirculation. There was a tendency toward decreased blood pressure (approximately 5 **mm** Hg) and increased pulse rate (approximately 5 beats/min), neither was clearly dose dependent. Oral bosentan was well tolerated. Vomiting and local intolerability was observed at the higher intravenous doses. CONCLUSION: Bosentan is an orally bioavailable, well-tolerated, and active ET-1 antagonist with a low clearance and a moderate volume of distribution. Its intravenous use is limited because of local intolerability.
Record Date Created: 19961029
Record Date Completed: 19961029
...; Endothelin-3--blood--BL; Endothelins--administration and dosage--AD; Heart Rate--drug effects--DE; Injections, **Intradermal** ; Injections, Intravenous; Protein Precursors--blood--BL; Reference Values; Skin--drug effects--DE; Sulfonamides--administration and...

21/7,K/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05877620 EMBASE No: 1994289126
Effect of estradiol on the sympathoadrenal response to mental stress in

normal men
Del Rio G.; Velardo A.; Zizzo G.; Avogaro A.; Cipolli C.; Della Casa L.; Marrama P.; MacDonald I.A.
Dept. of Internal Medicine Interna, Chair of Metabolism, Policlinico, Via del Pozzo 71,41100 Modena Italy
Journal of Clinical Endocrinology and Metabolism (J. CLIN. ENDOCRINOL. METAB.) (United States) 1994, 79/3 (836-840)
CODEN: JCEMA ISSN: 0021-972X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
It has been shown that steroid hormones are able to influence the sympathoadrenal system activity. Therefore, we have investigated in a double blind cross-over study the effect of percutaneous estradiol administration (100 mug) on the sympathoadrenal and cardiovascular responses to mental arithmetic stress in 20 normal young males. The **plasma** estradiol **level** was 154 +/- 14 pmol/L during the estrogen session (ES) and 44 +/- 7 pmol/L during the placebo session (PL; P < 0.001). The mental stress induced a significant increase in systolic blood pressure during both the PL (F = 7.2; P < 0.001) and the ES (F = 4.8; P < 0.01); the peak obtained during PL was, however, higher than that during ES (128 +/- 2 vs. 122 +/- 3 **mm** Hg; P < 0.02). A significant increase in pulse rate was observed during PL (F = 4.2; P < 0.002), but not during ES (F = 2.6; P = 0.47), with the peak pulse rate being higher during mental stress in the PL than the ES (78 +/- 2 vs. 74 +/- 2 beats/min; P < 0.03). In response to the mental stress, plasma epinephrine increased significantly during PL (F = 3.2; P < 0.03), but not during ES (F = 1.1; P = 0.3). The stress-induced peak in plasma epinephrine during PL was higher than that during ES when expressed as the absolute value or the incremental peak (513 +/- 103 vs. 125 +/- 32 pmol/L; P < 0.005). The incremental peak in plasma norepinephrine obtained during PL was higher than that during ES (0.78 +/- 0.1 vs. 0.27 +/- 0.07 nmol/L; P < 0.02). Plasma free fatty acid, acetoacetate, and 3-hydroxybutyrate increased significantly from basal values during PL, but not during ES. These data show that mildly elevated levels of estradiol are able to influence the response of the adrenal medulla to mental stress in men.
MEDICAL DESCRIPTORS:
...crossover procedure; dose response; double blind procedure; drug blood level; drug effect; human; human experiment; **intradermal** drug administration; male; normal human; obesity; priority journal; pulse rate; systolic blood pressure

21/7,K/4 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

00086201 EMBASE No: 1974076281
Pathophysiological studies in a case of severe orthostatic hypotension caused by systemic postganglionic denervation (Japanese)
Okada F.; Yamauchi T.; Kimura N.; Kunita H.
Dept. Psychiat. Neurol., Hokkaido Univ. Sch. Med., Sapporo Japan
CLIN.NEUROL. 1973, 13/6 (355-363)
CODEN: RISHB
DOCUMENT TYPE: Journal
LANGUAGE: JAPANESE
A 34 yr old male merchant suddenly became ill with upper abdominal pain, diarrhea and a sensation of heat and flushing of the abdomen and extremities. On the second day of his illness, it was noted that both

pupils were dilated and did not react to light. In the few days that followed, he experienced blurred vision while standing. He had several episodes of loss of consciousness when erect, with complete and rapid recovery upon lying down. Two months after the onset of disease, he showed orthostatic hypotension, syncope, heat intolerance, anhidrosis, nocturnal polyuria, impotence, youthful appearance and chronic diarrhea. The right pupil was 2.5 **mm** in diameter and irregular, and reacted very slightly to light. The left pupil was 3 **mm** in diameter and round, and reacted promptly to light. The instillation of 0.1% adrenaline into the conjunctival sac produced dilatation of the pupil on both sides. However, the instillation of 4% ephedrine did not produce such an effect. The local pilomotor phenomenon following **intradermal** 0.1% adrenaline appeared extensively in the extremities, but there was no response following **intradermal** 0.01% acetylcholine. The normal sweating response to heat and to pilocarpine was lost except on the face and neck. Skin biopsies revealed a slight decrease in the number of sweat glands in an area of anhidrosis. An extremely marked pressor response was elicited by adrenaline and noradrenaline, but there was no response to ephedrine. The orthostatic **increase** in **plasma** renin activity was abolished. These findings indicate that the lesion was located in the postganglionic sympathetic neurons. Instillation of 2.5% methacholine into the conjunctival sac caused an excessive response, suggesting that the site of disturbance lay also in the ciliary ganglion.

26/6/2 (Item 2 from file: 155)
04631526 PMID: 914655
Vascular reactions to horseradish peroxidase in the guinea pig.
Aug 22 1977

26/6/3 (Item 3 from file: 73)
01355117 EMBASE No: 1979075784
Analysis of intracutaneous inflammatory lesions with skin blisters. I. Cytological characterization and subclass distribution of lymphocytes infiltrating purified protein derivative-induced inflammatory lesions
1978

26/6/4 (Item 4 from file: 73)
02209258 EMBASE No: 1982064419
Ethiopathogenesis of nasal polyps: Are polyps of an allergic origin?
ETIOPATOGENIA DE LOS POLIPOS NASALES: SON LOS POLIPOS DE ORIGEN ALERGICO?
1981

26/6/5 (Item 5 from file: 35)
793980 ORDER NO: AAD82-23446
SPHINGOMYELINASE D FROM BROWN RECLUSE SPIDER (LOXOSCELES RECLUSA) VENOM: PURIFICATION AND CHARACTERIZATION
Year: 1981

26/6/6 (Item 6 from file: 73)
02307558 EMBASE No: 1983238719
Antihypertensive activity of dl-15-deoxy-16-hydroxy-16(alpha/beta)-vinyl prostaglandin Einf 2 methyl ester (CL 115,347), a new orally and transdermally long-acting antihypertensive agent
1983

26/6/7 (Item 7 from file: 73)

03100823 EMBASE No: 1986213400
Dexamethasone-suppressible hyperaldosteronism. Adrenal transition cell hyperplasia?
1986

26/6/8 (Item 8 from file: 155)
07354817 PMID: 3101414
Generation of immunoreactive neurotensin(s) and enkephalin(s) by pepsin-treatment of plasma .
1986

26/6/9 (Item 9 from file: 155)
07236448 PMID: 2428598
Pepsin treatment of mammalian plasma **generates immunoreactive and biologically active neurotensin-related peptides in micromolar concentrations.**
Oct 1986

26/6/10 (Item 10 from file: 155)
07424570 PMID: 2437111
Structure of a biologically active neurotensin-related peptide obtained from pepsin-treated albumin(s).
May 5 1987

26/6/12 (Item 12 from file: 155)
08511354 PMID: 2110012
2-substituted indazolinones: orally active and selective 5-lipoxygenase inhibitors with anti-inflammatory activity.
Jan 1990

26/6/13 (Item 13 from file: 155)
09014624 PMID: 1883775
Long duration local anesthesia with lecithin-coated microdroplets of methoxyflurane: studies with rat skin.
May-Jun 1991

26/6/16 (Item 16 from file: 73)
05068352 EMBASE No: 1992208568
Immunocytochemical and functional characterization of Nasup + conductance in adult alveolar pneumocytes
1992

26/6/18 (Item 18 from file: 155)
09305875 PMID: 1588290
Prolonged treatment with recombinant interferon gamma induces erythema nodosum leprosum in lepromatous leprosy patients.
Jun 1 1992

26/6/19 (Item 19 from file: 34)
02724374 Genuine Article#: LY791 Number of References: 30
Title: EFFECT OF A CALCITONIN-GENE-RELATED PEPTIDE ANTAGONIST (CGRP8-37) ON SKIN VASODILATATION AND EDEMA INDUCED BY STIMULATION OF THE RAT SAPHENOUS NERVE (Abstract Available)

26/6/20 (Item 20 from file: 155)
09766356 PMID: 8330926

Effect of a series of 1-alkyl ether lipids on inhibition of phospholipase A2 activity and PAF responses.
Jun 1993

26/6/21 (Item 21 from file: 155)
09592533 PMID: 8093894
Prolonged immunostimulatory effect of low-dose polyethylene glycol interleukin 2 in patients with human immunodeficiency virus type 1 infection.
Feb 1 1993

26/6/23 (Item 23 from file: 73)
05741649 EMBASE No: 1994148868
Cutaneous permeability responses to bradykinin and histamine in the guinea-pig: Possible differences in their mechanism of action
1994

26/6/24 (Item 24 from file: 34)
05101304 Genuine Article#: VA380 Number of References: 28
Title: THE VASODILATOR COMPONENT OF NEUROGENIC INFLAMMATION IS CAUSED BY A SPECIAL SUBCLASS OF HEAT-SENSITIVE NOCICEPTORS IN THE SKIN OF THE PIG
(Abstract Available)

26/6/25 (Item 25 from file: 155)
13305333 PMID: 8975870
Rabbit vascular endothelial adhesion molecules: ELAM-1 is most elevated in acute inflammation, whereas VCAM-1 and ICAM-1 predominate in chronic inflammation.
Dec 1996

26/6/26 (Item 26 from file: 155)
13128079 PMID: 8796283
Pharmacological characterization of novel tissue kallikrein inhibitors in vivo.
May 1996

26/6/27 (Item 27 from file: 34)
05705898 Genuine Article#: WR269 Number of References: 44
Title: Comparison of the reversed passive Arthus and local Shwartzman reactions of rabbit skin: Effects of the long-acting PAF antagonist UM-74,505 (ABSTRACT AVAILABLE)
Publication date: 19970400

26/6/28 (Item 28 from file: 155)
13592957 PMID: 9280370
Pharmacology of the 5-lipoxygenase inhibitors BAY Y 1015 and BAY X 1005 in the horse.
Aug 1997

26/6/31 (Item 31 from file: 34)
08955750 Genuine Article#: 349GR Number of References: 61
Title: Immune responses to a recombinant human immunodeficiency virus type 1 (HIV-1) gp160 vaccine among adults with advanced HIV infection (ABSTRACT AVAILABLE)
Publication date: 20000700

26/7,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04142175 PMID: 127605
The deoxyribonucleic acid (DNA) skin test in systemic lupus erythematosus. 2. Histological findings.
Johansson E A; Niemi K M; Lassus A
British journal of dermatology (ENGLAND) Oct 1975, 93 (4) p451-7, ISSN 0007-0963 Journal Code: 0004041
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A total of fifty-five biopsies from fifty-two **intradermal** DNA skin tests were studied. The biopsies were taken, 6, 8-10, 24 or 48 h after the injection of the DNA material. Necrosis of the vessel wall was taken to be the main characteristic of a specific reaction. In forty of the fifty-two tests the results of the histological evaluation closely matched the clinical results. In five of the fifteen cases with discrepancies, the histological evaluation ruled out clinically false positive test results. In three cases of SLE on corticosteroid treatment, the histological examination gave a positive result despite a clinically negative result. In seven of the fifteen cases the discrepancies occurred in borderline cases with reactions of 5 to 6 **mm** diameter. The amount of inflammatory cells in positive as well as in negative reactions was also recorded. The number of polymorphonuclear cells in positive reactions increased with the age of the reaction. The number of lymphocytes was not found to increase in the positive reactions, thus differing from the delayed hypersensitivity type of reactions. Rather, the reaction was characterized by an Arthus type of hypersensitivity. On the basis of the present study it may be concluded that clinically positive tests at 6 or 8 h may merely be expressions of nonspecific vascular alterations. On the other hand, in late reactions, even in patients on systemic treatment, histological examination revealed clinically negative results to be positive. By using the histological picture of hypersensitivity angiitis as the main diagnostic criterion the specificity of the clinical reactions may be established.
Record Date Created: 19760301
Record Date Completed: 19760301
...; Lupus Erythematosus, Systemic--immunology--IM; Lupus Erythematosus, Systemic--pathology--PA; Lymphocytes; Middle Aged; Necrosis; Neutrophils; **Plasma** Cells; Skin--blood supply--BS; Time Factors

26/7,K/11 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

04238041 EMBASE No: 1990120584
Administration of recombinant interleukin-2 reduces the local parasite load of patients with disseminated cutaneous Leishmaniasis
Akuffo H.; Kaplan G.; Kiessling R.; Teklemariam S.; Dietz M.; McElrath J.; Cohn Z.A.
Rockefeller University, 1230 York Ave.,New York, NY 10021-6399 United States
Journal of Infectious Diseases (J. INFECT. DIS.) (United States) 1990, 161/4 (775-780)
CODEN: JIDIA ISSN: 0022-1899
DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Three patients with disseminated cutaneous leishmaniasis received three intranodular injections of 10 mug of recombinant interleukin 2 (rIL-2) at 48-h intervals. After 7 and 14 days, 4- **mm** punch biopsies were taken of control and injected nodules and processed for histology, electron microscopy, immunocytochemistry, and parasite culture. Control sites exhibited loose infiltrates of parasitized macrophages and T cells predominantly of the CD8sup + phenotype. Amastigotes were present in large numbers and were found distributed within tightly apposed endosomes and larger vacuoles. After the administration of rIL-2, there was a prominent influx of T cells, predominantly of the CD4sup + phenotype, and an increased number of plasma cells. At 7 days, leishmanial amastigotes were present in either the same or somewhat reduced numbers but predominantly within large, lucent vacuoles. By 14 days the number of amastigotes were strikingly lower. Lymphokine-treated skin sites became sterile in two patients, as evaluated by parasite culture after rIL-2 injection. The results suggest that the local administration of rIL-2 induces a beneficial enhancement of the cellular immunity with a consequent disposal of parasites in the cutaneous site.

MEDICAL DESCRIPTORS:

adolescent; adult; amastigote; biopsy; cellular immunity; cytochemistry; electron microscopy; histology; lymphocyte proliferation; macrophage; parasite; **plasma** cell; promastigote; skin test; smear; t lymphocyte; ultrastructure; protozoon; case report; human; male; intradermal drug...

26/7,K/14 (Item 14 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08920056 PMID: 1675370

Administration of antidiuretic peptide (DDAVP) by way of suction de-epithelialised skin.

Svedman P; Lundin S; Svedman C

Department of Plastic and Reconstructive Surgery, University of Lund, Malmo, Sweden.

Lancet (ENGLAND) Jun 22 1991, 337 (8756) p1506-9, ISSN 0140-6736 Journal Code: 2985213R

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Transdermal drug delivery seems a promising way of achieving complete, predictable absorption, but the epidermis is a barrier for most drugs. A new technique for transdermal drug delivery, in which a small patch of epidermis was removed, was tested in seven healthy volunteers by means of the antidiuretic peptide 1-deamino-8-D-arginine vasopressin (DDAVP). The epithelium of a small area of forearm skin (diameter 5 **mm**) was removed painlessly, and in a standard way, by a simple device operating at a present vacuum. DDAVP was given by way of improvised occlusive reservoirs. **Plasma** DDAVP concentration/time curves conformed closely with zero-order kinetics, which suggests that the bioavailability approached 100%, corresponding to that for direct intravenous infusion. Four volunteers were given DDAVP daily for 4 days by way of the de-epithelialised site; there were no signs that re-epithelialisation hindered permeation. All **plasma** DDAVP values substantially exceeded the lowest effective therapeutic concentration for patients with diabetes insipidus. The vacuum removal of the epithelium caused pronounced hyperaemia in the de-epithelialised dermis

(assessed by laser doppler flow measurement); the hyperaemia persisted, unaffected by DDAVP, and may have contributed to the efficient permeation. The skin spot appeared normal at 6 weeks.
Record Date Created: 19910718
Record Date Completed: 19910718
...; BL; Desmopressin--pharmacokinetics--PK; Desmopressin--urine--UR; Diabetes Insipidus--drug therapy--DT; Evaluation Studies; Injections, **Intradermal** ; Microcirculation; Middle Aged; Skin Absorption; Suction --instrumentation--IS

26/7,K/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
08855959 PMID: 1826567
Immunogenicity of low-dose intradermal recombinant DNA hepatitis B vaccine.
Parish D C; Muecke H W; Joiner T A; Pope W T; Hadler S C
Department of Internal Medicine, Medical Center of Central Georgia, Macon 31208.
Southern medical journal (UNITED STATES) Apr 1991, 84 (4) p426-30, ISSN 0038-4348 Journal Code: 0404522
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial; Review; Review of Reported Cases
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Low-dose **intradermal** vaccination with plasma-derived hepatitis B vaccine has been shown to give high rates of seroconversion at greatly reduced vaccine cost. We report a study comparing two groups given lower doses (1.0 or 1.5 microgram) of recombinant-derived vaccine **intradermally** with a control group given the standard intramuscular dose. Of the 132 randomized medical students and hospital employees, 95 completed the study. Rates of seroconversion and peak antibody titers were comparable, though antibody rose more slowly and fell somewhat faster in the **intradermal** groups. Increasing the **intradermal** dose did not improve response. Most **intradermal** vaccinees (80%) developed small (average 2 to 3 mm) areas of local induration, which faded slowly. Low-dose **intradermal** vaccination with recombinant hepatitis B vaccine results in high rates of seroconversion (greater than 90% in each protocol) at a cost that will allow individual practitioners and program with limited budgets to offer vaccination. (37 Refs.)
Record Date Created: 19910510
Record Date Completed: 19910510
; Adult; Costs and Cost Analysis; Evaluation Studies; Hepatitis B Vaccines; Injections, **Intradermal** --adverse effects--AE; Injections, Intramuscular--adverse effects--AE; Middle Aged; Time Factors; Vaccination --economics--EC...

26/7,K/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.
09417799 PMID: 1512473
Microdialysis of the interstitial water space in human skin in vivo: quantitative measurement of cutaneous glucose concentrations.
Petersen L J; Kristensen J K; Bulow J
Department of Clinical Physiology, Bispebjerg University Hospital,

Copenhagen, Denmark.
Journal of investigative dermatology (UNITED STATES) Sep 1992, 99 (3) p357-60, ISSN 0022-202X Journal Code: 0426720
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The purpose of this study was to evaluate the usefulness of a microdialysis technique for measurement of substances in the interstitial water space in intact human skin. Glucose was selected to validate the method. The cutaneous glucose concentration was measured by microdialysis and compared to that in venous blood. Single dialysis fibers (length 20 **mm**, 2,000 Da molecular weight cutoff) were glued to nylon tubings and inserted in forearm skin by means of a fine needle. Dialysis fibers were inserted in duplicate. Seven subjects were investigated after an overnight fast. **Intradermal** position of the dialysis probes was established by C-mode ultrasound scanning. The implantation trauma lasted 90-135 min as measured by laser Doppler flowmetry. Each dialysis fiber was calibrated in vivo by perfusing it with four to five different glucose concentrations. The perfusion rate was 3 microliters/min. Regression analysis of the calibration curves yielded the relative in vivo recovery of glucose. The skin glucose concentration was calculated as that particular perfusate glucose concentration that resulted in no net glucose transport across the dialysis membrane. Correlation coefficient of the regression lines was 0.93 +/- 0.03 (mean +/- SEM). After the injection trauma had vanished, recovery was 20.5 +/- 0.7%. Coefficient of variation (CV) on recovery was 10.9%. The cutaneous glucose concentration was 99.1 +/- 1.8% of the glucose concentration in venous **plasma** water (CV 4.1%). These findings suggest that the microdialysis technique accurately and precisely can reflect biochemical events in the interstitial water space in human skin in vivo.

Record Date Created: 19920929
Record Date Completed: 19920929

26/7,K/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008883865 BIOSIS NO.: 199396048281
Binding of thrombospondin to human plasma **lipoproteins**
AUTHOR: Muraishi Akihiko; Capuzzi David M; Tuszynski George P
AUTHOR ADDRESS: Dep. Med., Med. Coll. Pennsylvania, 3300 Henry Avenue, Philadelphia, PA 19129, USA**USA
JOURNAL: Biochemical and Biophysical Research Communications 193 (3): p 1145-1151 1993
ISSN: 0006-291X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Immunohistochemical studies have localized thrombospondin (TSP), a platelet adhesive protein, to the atherosclerotic plaque. To investigate how TSP may become incorporated in the plaque, we evaluated the interaction of TSP with human plasma lipoproteins and apolipoproteins. Chylomicrons, VLDL, LDL, HDL, and apolipoproteins AI, AII, C were immobilized on microtiter plates. Binding to TSP was measured directly with (1251)TSP. Labeled TSP bound saturably to all the plasma lipoproteins tested, showing the highest capacity for binding to VLDL. This binding to VLDL was maximal in the presence of 1 mM CaCl-2 and

MgCl-2 and only partially inhibited with EDTA. The binding was inhibited totally by incubation with fluid-phase lipoproteins, apolipoproteins or anti-TSP monoclonal antibodies. The dissociation constants (Kd) for VLDL and apo C were 153 nM and 150 nM, respectively. Thus, TSP exhibits specific and saturable binding with high affinity to VLDL, perhaps mediated by its surface apo C. This binding may facilitate TSP incorporation into nascent atherosclerotic plaques and delivery of VLDL cholesterol into these lesions.

26/7,K/29 (Item 29 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08222098 Genuine Article#: 259CE Number of References: 54
Title: Dorsal root reflexes and cutaneous neurogenic inflammation after intradermal injection of capsaicin in rats
Author(s): Lin Q; Wu J; Willis WD (REPRINT)
Corporate Source: UNIV TEXAS,MED BRANCH, INST MARINE BIOMED, DEPT ANAT & NEUROSCI, 301 UNIV BLVD/GALVESTON//TX/77555 (REPRINT); UNIV TEXAS,MED BRANCH, INST MARINE BIOMED, DEPT ANAT & NEUROSCI/GALVESTON//TX/77555
Journal: JOURNAL OF NEUROPHYSIOLOGY, 1999, V82, N5 (NOV), P2602-2611
ISSN: 0022-3077 Publication date: 19991100
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE
Abstract: Dorsal root reflexes and cutaneous neurogenic inflammation after **intradermal** injection of capsaicin in rats. J. Neurophysiol. 82: 2602-2611, 1999, The role of dorsal root reflexes (DRRs) in acute cutaneous neurogenic inflammation induced by **intradermal** injection of capsaicin (CAP) was examined in anesthetized rats. Changes in cutaneous blood flow (flare) on the planter surface of the foot were measured using a laser Doppler flowmeter, and neurogenic edema was examined by measurements of paw thickness. To implicate DRRs in neurogenic inflammation after CAP injection, the ipsilateral sciatic and femoral nerves were sectioned, dorsal rhizotomies were performed at L3--S-1, and antagonists of GABA or excitatory amino acid receptors were administered intrathecally. Intradermal injection of CAP evoked a flare response that was largest at 15-20 **mm** from the injection site and that spread >30 mm. Acute transection of the sciatic and femoral nerves or dorsal rhizotomies nearly completely abolished the blood flow changes 15-20 mm from the CAP injection site, although there was only a minimal effect on blood how near the injection site. These procedures also significantly reduced neurogenic edema. Intrathecal bicuculline, 6-cyano-7-nitroquinoxaline-2,3-dione, (CNQX) or D(-)-2-amino-7-phosphonoheptanoic acid (AP7), but not phaclofen, also reduced dramatically the increases in blood flow 15-20 mm from the CAP injection site, but had only a minimal effect on blood how near the injection site. Neurogenic edema was reduced by the same agents that reduced blood flow. Multiunit DRRs recorded from the central stumps of cut dorsal rootlets in the lumbar spinal cord were enhanced after CAP injection. This enhanced DRR activity could be reduced significantly by posttreatment of the spinal cord with bicuculline, CNQX or AW, but not phaclofen. It is concluded that peripheral cutaneous inflammation induced by intradermal injection of CAP involves central nervous mechanisms. DRRs play a major role in the development of neurogenic cutaneous inflammation, although a direct action of CAP on peripheral nerve terminals or the generation of axon reflexes also may contribute to changes in the skin near the injection site.

26/7,K/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14367023 PMID: 10361615

Interstitial lactate levels in human skin at rest and during an oral glucose load: a microdialysis study.

Petersen L J
Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Denmark.

Clinical physiology (Oxford, England) (ENGLAND) May 1999, 19 (3) p246-50, ISSN 0144-5979 Journal Code: 8309768
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In vitro data have suggested that the skin is a significant lactate source. The purpose of the present study was to measure lactate and glucose concentrations in intact human skin in vivo using the microdialysis technique. Microdialysis fibres of 216 **microns** were inserted **intradermally** and perfused at a rate of 3 microliters min-1. In the first experimental protocol, dialysis fibres were calibrated by the method of no net flux in eight subjects. Skin lactate concentrations of 2.48 +/- 0.17 mmol l-1 were significantly greater than lactate concentrations of 0.84 +/- 0.15 mmol l-1 in venous plasma ($P < 0.01$). Glucose concentrations in skin and venous plasma were similar (5.49 +/- 0.18 vs. 5.26 +/- 0.24 mmol l-1). In the second experimental protocol, changes in lactate and glucose levels were studied in 10 subjects after an oral glucose tolerance test (OGTT). After the OGTT, plasma glucose and lactate levels increased by 54% and 39% to peak levels at 30 and 60 min respectively. In comparison, skin glucose and lactate increased by 41% and 18% at 60 and 90 min. No changes in skin blood flow were observed during the OGTT. The data suggest that resting skin is a significant lactate source with no significant lactate production during OGTT. The cellular source of lactate in the skin remains undetermined to date.

Record Date Created: 19990728
Record Date Completed: 19990728

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File  98:General Sci Abs/Full-Text 1984-2004/May
File   9:Business & Industry(R) Jul/1994-2004/Jun 03
File  16:Gale Group PROMT(R) 1990-2004/Jun 04
File 160:Gale Group PROMT(R) 1972-1989
File 148:Gale Group Trade & Industry DB 1976-2004/Jun 04
File 621:Gale Group New Prod.Annou.(R) 1985-2004/Jun 02
File 149:TGG Health&Wellness DB(SM) 1976-2004/May W4
File 636:Gale Group Newsletter DB(TM) 1987-2004/Jun 03
File 441:ESPICOM Pharm&Med DEVICE NEWS 2004/May W5
File 369:New Scientist 1994-2004/May W5
File 370:Science 1996-1999/Jul W3
File 135:NewsRx Weekly Reports 1995-2004/May W4
File 129:PHIND(Archival) 1980-2004/May W5
File 455:Drug News & Perspectives 1992-2004/Apr
File 481:DELPHES Eur Bus 95-2004/May W4
File 624:McGraw-Hill Publications 1985-2004/Jun 03
File 635:Business Dateline(R) 1985-2004/Jun 04
Set     Items   Description
S1       2714   INTRADERMAL? OR INTRA()DERMAL? OR INTRAEPIDERMAL? OR INTRA-
             ()EPIDERMAL?
S2      79640   NEEDLE? ? OR MICRONEEDLE? ?
S3     656074   OUTLET? ?
S4     492264   MM OR MILLIMETER? ? OR MILLIMETRE? ? OR UM OR MICRON? ? OR
            MICROM? ? OR MICROMETER? ? OR MICROMETRE? ?
S5     141908   PLASMA
S6        259   (S1 OR S2(2N)S3)(S)S4
S7         18   S5(S)S6
S8         16   RD (unique items)
S9          0   S8/2001:2004
S10        16   Sort S8/ALL/PD,A

10/3,AB,K/1     (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
(c) 2004 The Gale Group. All rts. reserv.
01236603     SUPPLIER NUMBER: 08918321    (USE FORMAT 7 OR 9 FOR FULL TEXT)
Chronic urticaria.
Burrall, Barbara A.; Halpern, Georges M.; Huntley, Arthur C.
The Western Journal of Medicine, v152, n3, p268(9)
March, 1990
PUBLICATION FORMAT: Magazine/Journal   ISSN: 0093-0415  LANGUAGE: English
RECORD TYPE: Fulltext; Abstract  TARGET AUDIENCE: Professional
WORD COUNT:   7754    LINE COUNT:  00681
ABSTRACT: Urticaria is a blood vessel reaction of the skin characterized
by the eruption or outbreak of pale, transient wheals or elevations of the
skin, which are associated with severe itching. This skin condition affects
15 to 20 percent of the population and occurs in various forms. Urticaria
may result from exposure of the skin to fresh or salt water, cold, heat,
sun, irritants, and certain medications. This skin disorder is also
classified by the characteristics of the skin lesion, which may occur as
blisters, blood-containing hives, or red lesions and may be associated with
pimples or accumulation of mast cells, which are important in cell defense
mechanisms. The chronic form of urticaria recurs frequently and lasts more
than six weeks. The cause of chronic urticaria is unknown in 75 percent of
cases, but may be related to effects of various types of natural factors
released in the body. Urticaria associated with angioedema, or swelling of
the skin, may result from abnormalities of the immune system, or may result
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from nonimmune causes. The various types of urticaria require proper evaluation and specific treatment. Drugs used to treat urticaria include antihistamines and corticosteroids. Antihistamines block the actions of histamine, a natural substance that is involved in several cell processes, including dilation of blood vessels, while corticosteroids prevent the inflammation of the skin. Antihistamines that cause drowsiness should only be given to patients who develop hives at night. (Consumer Summary produced by Reliance Medical Information, Inc.)
AUTHOR ABSTRACT: Urticaria affects 15% to 20% of the population once or more during a lifetime. Chronic urticaria is a frequent recurrent eruption over a period greater than 6 weeks; the cause remains a mystery in more than 75% of cases. Urticaria and angioedema may be produced by immunologic or nonimmunologic means. Urticarial vasculitis, contact urticaria, mastocytosis, physical urticarias, dermatographism, cholinergic urticaria, localized heat urticaria, cold urticaria, aquagenic urticaria, and vibratory angioedema all require specific evaluation and treatment. Chronic idiopathic urticaria is usually controlled by antihistamines; depending on the circadian rhythm of the eruption, sedative or nonsedative antihistamines are prescribed. Some patients will require a combination of H, and H2 antagonists, or even parenteral corticosteroids. (Burrall BA, Halpern GM, Huntley AC: Chronic urticaria. West J Med 1990 Mar; 152:268-276)

10/3,AB,K/2 (Item 2 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

05204166 SUPPLIER NUMBER: 10948943 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Reversal of nonresponders and postexposure prophylaxis by intradermal hepatitis B vaccination in Japanese medical personnel.
Nagafuchi, Seiho; Kashiwagi, Seizaburo; Okada, Kenji; Anzai, Keizo; Nakamura, Minoru; Nishimura, Yasuharu; Sasazuki, Takehiko; Niho, Yoshiyuki
JAMA, The Journal of the American Medical Association, v265, n20, p2679(5)
May 22, 1991
ISSN: 0098-7484 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 3735 LINE COUNT: 00309
ABSTRACT: Hepatitis B is the ninth leading cause of death worldwide. The virus is spread by exposure to contaminated blood, sexual contact with an infected person, or by infected mothers who pass the virus to their babies at birth. Health care workers are at high risk for infection because of contact with needles and the blood of infected patients. Although the hepatitis B vaccine is effective, it is expensive, takes a long time to provide immunity, and provides incomplete protection after exposure to the virus. The duration of immunity is unpredictable, and some people fail to develop immunity. Injection of the vaccine under the skin (intradermal injection) provides good results at a lower cost than injection into the muscle (intramuscular injection). Another advantage of the intradermal vaccine is the formation of delayed type hypersensitivity (DTH) skin reaction, which indicates whether the vaccine was effective. In addition, intradermal injection reverses nonresponsiveness to the vaccine among individuals who did not benefit from intramuscular injection. Thirty-one Japanese health care workers who did not respond to injections of the conventional vaccine were given the intradermal vaccine. Nonresponsiveness was reversed in 94 percent, and long-lasting immunity resulted. Women required fewer revaccinations, and older people responded less well than their younger counterparts. Intradermal hepatitis B vaccine is useful for vaccinating nonresponders at high risk for exposure and for preventive

vaccination after exposure. This method may be useful against other viruses with long incubation periods, including rabies, hepatitis C, and human immunodeficiency virus. (Consumer Summary produced by Reliance Medical Information, Inc.)
... hepatitis B DNA polymerase activity, and nine had positive results) were given 5 [Lg of **plasma** -derived hepatitis B vaccine **intradermally** every 2 weeks until the DTH skin reaction became positive. At the initial injection, erythematous...
...erythema but no development of induration. In positive reactions, an induration of more than 3 **mm** developed 48 hours after injection, indicating the development of an active immunity, which was regarded...

10/3,AB,K/3 (Item 3 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB
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05193922 SUPPLIER NUMBER: 10916829 (USE FORMAT 7 OR 9 FOR FULL TEXT)
New autonomic and sensory neuropathy with loss of adrenergic sympathetic function and sensory neuropeptides.
Anand, P.; Rudge, P.; Mathias, C.J.; Springall, D.R.; Ghatei, M.A.; Naher-Noe, M.; Sharief, M.; Misra, V.P.; Polak, J.M.; Bloom, S.R.; Thomas, P.K.
Lancet, v337, n8752, p1253(2)
May 25, 1991
ISSN: 0099-5355 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT
WORD COUNT: 1666 LINE COUNT: 00137
... on standing, which fell further on exercise, and could be as low as 40/20 **mm** Hg without causing loss of consciousness. Supine resting blood pressure was 102-108 **mm** Hg (heart rate 70-72 per min), falling to 75-86 (85-87 beats/min...
...taken orally improved the blood pressure for 4 h, with a peak of 150/85 **mm** Hg supine, and without a significant postural fall. Ingestion of L-DOPA and L-DOPS was followed by measurable concentrations of **plasma** dopamine and noradrenaline, respectively. Sweet tests were normal. Pupillometry confirmed sympathetic dysfunction. Skin flare testing, with 0.03 ml of histamine (1 mg/ml) injected **intradermally** into the forearm, [4] showed a normal wheal but diminished flare response (8 and 6...

10/3,AB,K/4 (Item 4 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB
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05456151 SUPPLIER NUMBER: 11295775 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Immunogenicity of low-dose intradermal recombinant DNA hepatitis B vaccine. (South Med J, 1991; 84:426-430) (Abstract)
JAMA, The Journal of the American Medical Association, v266, n6, p780(1)
August 14, 1991
DOCUMENT TYPE: Abstract ISSN: 0098-7484 LANGUAGE: ENGLISH
RECORD TYPE: FULLTEXT
WORD COUNT: 195 LINE COUNT: 00016
Low-dose **intradermal** vaccination with **plasma** -derived hepatitis B vaccine has been shown to give high rates of servoconversion at greatly...
...two groups given lower doses (1.0 or 1.5 pg) of recombinant-derived vaccine **intradermally** with a control group given the standard intramuscular dose. Of the 132 randomized medical students...
...antibody titers were comparable, though antibody rose more slowly and fell somewhat faster in the **intradermal** groups. Increasing the **intradermal** dose did not improve response. Most **intradermal** vaccines

(80%) developed small (average 2 to 3 **mm**) areas of local induration, which faded slowly. Low-dose **intradermal** vaccination with recombinant hepatitis B vaccine results in high rates of seroconversion ([is greater than...

10/3,AB,K/6 (Item 6 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

06176004 SUPPLIER NUMBER: 13211440 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Allergic skin disorders and mastocytosis. (Primer on Allergic and Immunologic Diseases, 3rd ed., Chapter 8)
Horan, Richard F.; Schneider, Lynda C.; Sheffer, Albert L.
JAMA, The Journal of the American Medical Association, v268, n20, p2858(11)
Nov 25, 1992
ISSN: 0098-7484 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 11646 LINE COUNT: 01025
ABSTRACT: Urticaria (hives) and angioedema are relatively common. They may be caused by food or drugs and involve the production of IgE antibody. Another form involves activation of the complement system and can occur weeks after the administration of the drug. Hereditary angioedema is characterized by swelling of the skin, respiratory tract and gastrointestinal system. It has no apparent cause. Some physical agents such as cold, heat, sunlight or exercise can also cause urticaria. Atopic dermatitis is a chronic skin disease involving IgE production. Contact dermatitis is an allergic reaction to topical medications, industrial chemicals, cosmetics and other agents. It involves activation of T cells. Mastocytosis is characterized by the proliferation of mast cells. When this occurs in the skin, the result is urticaria pigmentosa.
... treatment may be necessary.
Cholinergic urticaria is characterized by intensely pruritic, puncrate (1- to 3- **mm** diameter), blanched papules surrounded by erythematous flares and occurs in association with elevations of core...
...but wheezing is uncommon as a clinical concomitant. In the experimentally induced attack, elevation of **plasma** histamine levels and elaboration of eosinophilotactic peptides and neutrophil chemotactic factor have been documented. Ultrastructural...
...cholinergic discharge resulting from a central trigger caused by perceived core body temperature elevation. Methacholine **intradermal** skin test reproduces the clinical lesion. Treatment consists of avoidance of the provocative elevations in...

10/3,AB,K/7 (Item 7 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

06799749 SUPPLIER NUMBER: 14658380 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Hepatitis B vaccine responsiveness in Connecticut public safety personnel.
Roome, Aaron J.; Walsh, Stephen J.; Cartter, Matthew L.; Hadler, James L.
JAMA, The Journal of the American Medical Association, v270, n24, p2931(4)
Dec 22, 1993
ISSN: 0098-7484 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 3488 LINE COUNT: 00319
ABSTRACT: Age and obesity are among the factors that appear to influence the effectiveness of hepatitis B vaccine. Hepatitis B infection is caused by a blood-borne virus. Vaccination against hepatitis B is routinely offered to public safety employees such as firefighters, emergency medical technicians and police. The effectiveness of hepatitis B vaccine was

evaluated in 528 public employees, primarily firefighters, in Connecticut. All participants received the complete series of three doses of the vaccine. Blood samples were taken between one and six months after vaccination. Participants also completed questionnaires about their health status and their use of alcohol and tobacco. Nearly 12% of participants were inadequately protected by the vaccine. A high body mass index, increasing age, a history of smoking and an increase in time since vaccination were all associated with inadequate protection against the virus. Post-vaccination testing for immunity to hepatitis B should be performed routinely between 30 and 90 days after the last dose is given. AUTHOR ABSTRACT: Objective.--To determine the level and determinants of vaccine response in recently inoculated public safety personnel. Design.--Prevalence survey. Participants.--Public safety personnel who had completed vaccination 1 to 6 months prior to testing and had no serological evidence of previous exposure to hepatitis B virus. Main Outcome Measure.--An inadequate level of antibody to hepatitis B surface antigen was defined as less than 10 mIU/mL. Results.--All subjects in the study had been vaccinated using Recombivax HB, a recombinant hepatitis B vaccine. Of 528 individuals, 11.9% were found to have no or inadequate levels of antibody. The frequency of inadequate level of antibody increased significantly relative to age, from 2.8% among those younger than 30 years to 42.1% among those older than 60 years (P<.0001). Smoking (odds ratio [OR], 3.6; 95% confidence interval [CI], 2.0 to 6.4), extreme obesity (OR, 13.3; 95% CI, 3.8 to 49.1), and increasing time interval since completing the vaccine series (P<.01) were also associated with inadequate levels of antibody. These findings were confirmed by multivariate analysis using logistic regression. Conclusions.--Routine immunization of public safety personnel should include selective use of postvaccine testing. Postvaccination testing optimally should be performed in the 30- to 90-day interval after the last vaccine dose. New vaccination strategies are needed to improve response rates in persons with predictably poor response to hepatitis B vaccine.

10/3,AB,K/10 (Item 10 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports
(c) 2004 NewsRx. All rts. reserv.
0000006577 (USE FORMAT 7 OR 9 FOR FULLTEXT)
"PPD Response and HIV Viral Burden among HIV Infected IDUs."
TB & Outbreaks Week, February 27, 1995, p.10
DOCUMENT TYPE: Research News LANGUAGE: English
RECORD TYPE: FULLTEXT
WORD COUNT: 393
...TEXT: February 2, 1995, in Washington, DC, "Objective: To examine the relationship between PPD reactivity and **plasma** HIV viral burden. Methods: HIV infected injecting drug users (IDUs) were given **intradermal** skin tests with tuberculin (PPD), Candida, mumps, and tetanus antigens; for all tests, responses of greater than or equal to2 **mm** induration were detectable, and a PPD response greater than or equal to5 **mm** was considered indicative of TB infection. Cases (persons with a PPD response 22 **mm** but free of active TB disease) were randomly matched to 21 control by skin test...
...and response to each of the other skin tests (detectable or not). HIV RNA in **plasma** drawn at the skin test visit was measured using branched DNA (bDNA) signal amplification (Chiron...
...eq/ml) were observed in 88% (7/8) of persons with 0-199 CD4 cells/ **mm** 3 , 42% (18/43) of those with 200-399 cells/ **mm** 3 , and 13% (8/61) of those

with 2400 CD4 cells/ **mm** 3 The median detectable bDNA level was 17.5x10 3 eq/ml (range 10.5...
...Among cases, bDNA was detected more often in those with greater than or equal to5 **mm** PPD induration (23%, 8/35) than in the 24 **mm** group (12%, 2/17) (P =0.47, Fisher's exact test). Conclusions: In this cross...

10/3,AB,K/14 (Item 14 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports
(c) 2004 NewsRx. All rts. reserv.
0000004266 (USE FORMAT 7 OR 9 FOR FULLTEXT)
"PPD Response and HIV Viral Burden Among HIV Infected Injecting Drug Users Without Active TB."
AIDS Weekly, June 12, 1995, p.19
DOCUMENT TYPE: Research News LANGUAGE: English
RECORD TYPE: FULLTEXT
WORD COUNT: 405
...TEXT: burden among HIV-seropositive injecting drug users (IDUs) without active TB disease. Participants were given **intradermal** skin tests with PPD, Candida, mumps, and tetanus antigens; for all tests, responses of 22 **mm** induration were detectable. Cases (persons with a PPD response greater than or equal to2 **mm** but free of active TB) were randomly matched to greater than or equal to1 control...
...and response to each of the other skin tests (detectable or not). HIV RNA in **plasma** drawn at the skin test visit was measured using branched DNA (bDNA) signal amplification (Chiron...
...RNA eq/ml) were observed in 88% (7/8) of persons with <200 CD4 cells/ **mm** 3 , 42% (18/43) of those with 200-399 cells/ **mm** 3 , and 13% (8/61) of those with greater than or equal to400 CD4 cells/ **mm** 3 The median detectable bDNA level was 17.5x10 3 eq/ml (range 10.5...
...Among cases, bDNA was detected more often in those with greater than or equal to5 **mm** PPD induration (23%, 8/35) than in the 2-4 **mm** group (12%, 2/17) (P=0.47, Fisher's exact test). In this cross-sectional...

10/3,AB,K/15 (Item 15 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
(c) 2004 The Gale Group. All rts. reserv.
01525601 SUPPLIER NUMBER: 17143086 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Receptor endocytosis and dendrite reshaping in spinal neurons after somatosensory stimulation.
Mantyh, Patrick W.; DeMaster, Eric; Malhotra, Amit; Ghilardi, Joseph R.; Rogers, Scott D.; Mantyh, Christopher R.; Lui, Hantao; Basbaum, Allan I.; Vigna, Steven R.; Maggio, John E.; Simone, Donald A.
Science, v268, n5217, p1629(4)
June 16, 1995
PUBLICATION FORMAT: Magazine/Journal ISSN: 0036-8075 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic
WORD COUNT: 3068 LINE COUNT: 00254
AUTHOR ABSTRACT: In vivo somatosensory stimuli evoked the release of substance P from primary afferent neurons that terminate in the spinal cord and stimulated endocytosis of substance P receptors in rat spinal cord neurons. The distal dendrites that showed substance P receptor internalization underwent morphological reorganization, changing from a tubular structure to one characterized by swollen varicosities connected by thin segments. This internalization and dendritic structural reorganization provided a specific image of neurons activated by substance P. Thus receptor internalization can drive reversible structural changes in central

nervous system neurons in vivo. Both of these processes may be involved in neuronal plasticity.
... Krenning, S. W. J. Lamberts, Metabolism 39 (suppl. 2), 78 (1990); J. J. Bowden et al ., Proc. Nat. Acad. Sci, U.S.A. 91, 8964 (1994); A. M. Garland, E. F...

10/3,AB,K/16 (Item 16 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

08608066 SUPPLIER NUMBER: 18171856 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Effect of treatment with zileuton, a 5-lipoxygenase inhibitor, in patients with asthma: a randomized controlled trial.
Israel, Elliot; Cohn, Judith; Dube, Louise; Drazen, Jeffrey M.
JAMA, The Journal of the American Medical Association, v275, n12, p931(6)
March 27, 1996
ISSN: 0098-7484 LANGUAGE: English RECORD TYPE: Fulltext; Abstract
WORD COUNT: 5715 LINE COUNT: 00465
ABSTRACT: A new drug called zileuton may be an effective treatment for asthma. Zileuton belongs to a class of drugs that inhibit an enzyme involved in the synthesis of leukotrienes, which are inflammatory chemicals produced by the body. Researchers randomized 320 asthma patients to receive 600 milligrams (mg) of zileuton, 400 mg or a placebo four times a day for 13 weeks. Zileuton reduced the number of exacerbations requiring corticosteroids or beta-agonists and improved pulmonary function. It also increased the number of symptom-free days and nights and improved the quality of life overall. The higher dose provided greater benefits and was not associated with more adverse effects than the lower dose. Eight patients taking the drug experienced temporary abnormalities in liver function, which returned to normal following completion of the study.
AUTHOR ABSTRACT: Objective.--To study the effect of 3 months of treatment with zileuton, an inhibitor of the enzymatic pathway (5-lipoxygenase) leading to leukotriene formation, on disease control in patients with mild to moderate asthma. Design.--Randomized, double-blind, parallel-group study in 401 patients. A 10-day placebo lead-in was followed by a double-blind treatment period of 13 weeks. Setting.--Asthma study clinics in university hospitals and private practices. Patients or Other Participants.--Patients with mild to moderate asthma (forced expiratory volume in the first second ((FEV.sub.1)), 40% to 80% of predicted) whose only treatment was inhaled (beta)-agonists. Interventions.--Treatment with 600 mg or 400 mg of zileuton or placebo (each taken four times daily). Main Outcome Measures.--Frequency of asthma exacerbation requiring treating with corticosteroids, use of inhaled (beta)-agonists, pulmonary function tests, asthma symptom assessment, and quality-of-life evaluation. Safety was evaluated by monitoring adverse events. Results.--Only eight (6.1%) of 132 patients receiving 600 mg of zileuton four times a day required corticosteroid treatment for asthma vs 21 (15.6%) of 135 patients receiving placebo (P=.02), giving a relative risk of 2.6. At the time of expected peak drug concentration, the average (FEV.sub.1) improved 15.70/o in the 600-mg zileuton group vs 7.7% in the placebo group (P=.006). Quality-of-life assessments significantly improved in the 600-mg zileuton group and not in the placebo group P=.007 for the overall score). Elevations in liver function tests (more than three times normal), all of which reversed with drug withdrawal, occurred in five patients P=.03 vs placebo), three patients (P=.12 vs placebo), and no patients treated with 600 mg of zileuton, 400 mg of zileuton, or placebo, respectively. Conclusions.--Three months of 5-lipoxygenase inhibition produced a

significant improvement in asthma control. These data indicate that 5-lipoxygenase products of arachidonic acid metabolism are mediators of inflammation with an important role in the biology of asthma. (JAMA 1996;275:931-936)
... leukotriene C4 by human eosinphilis. J Immunol. 1987;138:532-538. (3.) Brown P, Monick MM , Hunninghake GW. Human alveolar macrophage arachidonic acid metabolism. Am J Physiol. 1988%W:C8O9-C815...
...sulfido-peptide leukotrienes in human subjects. Chest. 1986; 89:414-419. (5.) Adelroth E, Morris MM , Hargreave FE, O'Byrne PM. Airway responsiveness to leukotrienes C4 and D4 and to methacholine...
...Respir Dis. 1985; 131:368-372. (7.) Dahlen SE, Bjork J, Hedqvist P. Leukotrienes promote **plasma** leakage and leukocyte adhesion in postcapillary venules: in vivo effects with relevance to the acute...
...Black PN, Dollery CT. Effect of the oral leukotriene D4 antagonist LY171883 on inhaled and **intradermal** challenge with antigen and leukotriene D4 in atopic subjects. J Alkmy Clin Immunol. 1989;83...

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File 350:Derwent WPIX 1963-2004/UD,UM &UP=200434
File 347:JAPIO Nov 1976-2004/Jan(Updated 040506)
File 371:French Patents 1961-2002/BOPI 200209
Set     Items   Description
S1       5996   INTRADERMAL? OR INTRA()DERMAL? OR INTRAEPIDERMAL? OR INTRA-
             ()EPIDERMAL?
S2     116212   NEEDLE? ? OR MICRONEEDLE? ?
S3     415697   OUTLET? ?
S4     485370   MM OR MILLIMETER? ? OR MILLIMETRE? ? OR UM OR MICRON? ? OR
           MICROM? ? OR MICROMETER? ? OR MICROMETRE? ?
S5     233826   PLASMA
S6      97474   IC=(A61M031 OR A61M-037 OR A61M-005 OR A61K-000 OR A61K-03-8)
S7         45   (S1 OR S2(3N)S3) AND S4 AND S5
S8         20   S6 AND S7
S9         25   S7 NOT S8
```

8/26,TI/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015716970
WPI Acc No: 2003-779170/200373

New carboxy derivatives of isoflavone, useful for treating or diagnosing diseases e.g. cancer, cardiovascular disease and osteoporosis

8/26,TI/3 (Item 3 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015565188
WPI Acc No: 2003-627345/200359

Composition useful for treatment of HIV infection comprises e.g. compound capable of causing formation of cells capable of displaying HIV late-domain phenotype and adjuvant capable of stimulating cytotoxic T lymphocytes response

8/26,TI/4 (Item 4 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015430035
WPI Acc No: 2003-492177/200346

Novel anticoagulant peptide derived from the amino acid region 307-356 of human blood clotting factor Va, useful for preventing thrombotic disorders resulting from formation of blood clots that obstruct blood vessels

8/26,TI/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015342163
WPI Acc No: 2003-403101/200338

Novel thrombopoietin mimetic peptides which bind to mpl receptor, and which stimulate the production of platelets and/or the production of platelet precursors, useful for treating thrombocytopenia

8/26,TI/6 (Item 6 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015281591

WPI Acc No: 2003-342523/200332
Composition for treatment of a vascular tumor or hyperplastic tissue comprises a solid-phase agent containing a platelet specific component capable of binding platelets onto solid phase agent to induce platelet activation

8/26,TI/8 (Item 8 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014939085
WPI Acc No: 2002-759794/200282
New aminomethyl-pyrroloquinazoline compounds are thrombin receptor antagonists useful in the treatment of e.g. osteoporosis

8/26,TI/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014929722
WPI Acc No: 2002-750431/200281
Generating a modified protein with reduced antigenicity for treating cancer, AIDS, autoimmune diseases, comprises identifying a protein region antigenic in the first subject using antiserum from either the first or a second subject

8/26,TI/10 (Item 10 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014912120
WPI Acc No: 2002-732826/200279
New peptides antagonizing insulin-like growth factor (IGF), useful for treating disorder such as cancer, diabetic complication exacerbated by IGF-1, acromegaly, age-related macular degeneration, ischemic injury, trauma, asthma

8/26,TI/11 (Item 11 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014706777
WPI Acc No: 2002-527481/200256
Novel apolipoprotein construct comprising apolipoprotein A linked to carbohydrate, peptide or protein heterologous group, useful for treating plaque/unstable angina pectoris, myocardial infarction, arterial stenoses

8/26,TI/13 (Item 13 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014343595
WPI Acc No: 2002-164298/200221
Use of isatin-beta-thiosemicabazone and/or its 1-N-ethyl-derivative in the preparation of a medicament for the treatment of Herpes Simplex virus infection

8/26,TI/14 (Item 14 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014310024
WPI Acc No: 2002-130727/200217

Novel multimeric human tumor necrosis factor delta or epsilon protein useful for treating cancer, immune system disorders, infection, cardiovascular disorders, liver disease, cardiomyopathy, diabetes and psoriasis

8/26,TI/15 (Item 15 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014309419
WPI Acc No: 2002-130122/200217
New therapeutic MA polypeptides corresponding to human chorionic gonadotrophin peptides, useful for treating and preventing cancers, pathological angiogenesis and loss of body cell mass

8/26,TI/16 (Item 16 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014245697
WPI Acc No: 2002-066397/200209
Treatment of central nervous system injuries or diseases comprises administering at least one lipoic acid

8/26,TI/17 (Item 17 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014198539
WPI Acc No: 2002-019236/200203
New percyquinnin or its salt and derivatives in their stereoisomeric and tautomeric forms useful as lipolyse inhibitors for treating atherosclerosis, hypertension or diabetes

8/26,TI/18 (Item 18 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
013741559
WPI Acc No: 2001-225789/200123
Packaged formulation for treating a hormone dependent cancer, e.g. prostate cancer includes a solid ionic complex of a luteinizing hormone releasing hormone analogue and a carrier macromolecule

8/26,TI/19 (Item 19 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
013333862
WPI Acc No: 2000-505801/200045
Treating HIV infection, particularly resistant HIV infection, by administering beta-D-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine in combination with certain drugs that induce mutations in HIV-1

8/26,TI/20 (Item 20 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
013294052
WPI Acc No: 2000-465987/200040
Human Ckbeta-10 deletion mutants and nucleic acid sequences encoding them, used to prevent, treat, and ameliorate diseases such as rheumatoid arthritis, inflammatory disorders and cardiovascular diseases

8/34/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015160921
WPI Acc No: 2003-221449/200321
Administration of substance e.g. human growth hormone to produce improved systemic absorption comprises injecting substance into dermis
Patent Assignee: PHARMACIA CORP (PHAA); PINKERTON T C (PINK-I)
Inventor: PINKERTON T C; PINKERTON T
Number of Countries: 098 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200302175	A2	20030109	WO 2001US50862	A	20011226	200321 B
US 20030073609	A1	20030417	US 2001897801	A	20010629	200329
NO 200305580	A	20031215	WO 2001US50862	A	20011226	200412
			NO 20035580	A	20031215	
EP 1399205	A2	20040324	EP 2001991616	A	20011226	200421
			WO 2001US50862	A	20011226	

Priority Applications (No Type Date): US 2001897801 A 20010629
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200302175	A2	E	27	A61M-005/158	
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW				
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
US 20030073609	A1			A61K-038/28	
NO 200305580	A			A61M-000/00	
EP 1399205	A2	E		A61M-005/158	Based on patent WO 200302175
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

Abstract (Basic): WO 200302175 A2

NOVELTY - Administration of a substance comprises injecting the substance into the dermis to produce improved systemic absorption relative to absorption produced upon injecting the substance subcutaneously i.e. bolus subcutaneously. The substance is a growth hormone, a low molecular weight heparin or a dopamine receptor agonist.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a device (preferably an electroporation injection system or a thermal poration injection system) for administering a composition comprising a growth hormone, a low molecular weight heparin or a dopamine receptor agonist that configure selective delivery of the composition into the dermis.

USE - Used for administration of a substance (e.g. human hormone, low molecular weight heparin or dopamine receptor agonist) into the dermis (claimed).

In tests, six Yucatan mini-pigs received Fragmin (low molecular weight heparin fragment) (I) (2500 IU) by the following routes: (a) subcutaneous injection (SC), (b) **intradermal** (ID) injection by a needle of length 1 **mm** , and (c) **intradermal** injection by a needle of length 0.5 **mm**0 . Blood samples were obtained at different times and **plasma** concentration (ng/ml) of (I) was measured. The pharmacokinetic parameters using routes (a)/(b)/(c) were as follows: Cmax

(IU/ml)=0.6+/-0.3/1.1+/-0.1/1.5+/-0.3; Tmax (hour)=1+/-3.6/1+/-0.3/0.8+/-0.3; AUC/dose=0.018/0.023/0.033; T1/2 (hour)=9.3+/-4.9/2.9+/-0.5/6.5+/-5.5, and CL/F (mL/hourxkg)=31.4+/-11.3/37.6+/-3.4/27.2+/-8.9.

ADVANTAGE - The method improves systemic absorption compared to absorption produced on subcutaneous, intramuscular or other non-IV parenteral delivery of the substance. The method gives a shorter Tmax, higher bioavailability, more rapid uptake rate, more rapid onset of pharmacodynamics and biological effects, and reduced drug depot effects. The method reduces degradation of drugs and diagnostic agent and undesired immunogenic activity. The method involves directly targeting absorption by the papillary dermis by controlled delivery of drugs to dermal space of skin. As the method enhances the bioavailability, the equivalent biological effect can be obtained by using less active agent, providing direct economic benefit for expensive protein therapeutics and diagnostics and reducing overall dosing and side effects associated with higher dosing. The method has no change in systemic elimination rate or intrinsic clearance mechanism of drugs or diagnostic agents.

pp; 27 DwgNo 0/11

Technology Focus:

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The substance is injected through at least one hollow needle, by electroporation or by thermal poration (preferably by hallow needle comprising an array of microneedles).

Preferred Substance: The substance is in the form of nanoparticles.

Extension Abstract:

ADMINISTRATION - The substance is administered in a dosage of 100 mug/ml at a rate of 100 micro-l per minute over 5 minutes. The substance is administered by bolus injection (preferably repeated bolus injection) (claimed) into the **intradermal** layer of the skin.

Derwent Class: B05; B07; P34

International Patent Class (Main): **A61K-038/28** ; A61M-000/00; **A61M-005/158**

International Patent Class (Additional): A61K-031/00; A61K-031/727; **A61K-038/19** ; **A61K-038/27** ; A61M-001/00

8/34/12 (Item 12 from file: 350)

DIALOG(R)File 350:Derwent WPIX

014668945

WPI Acc No: 2002-489649/200252

Biphasic injectable composition for tissue volume replacement and as material in plastic and reconstructive surgery, comprises solid polymer phase and carrier substrate phase

Patent Assignee: DYER W K (DYER-I)

Inventor: DYER W K

Number of Countries: 097 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200217816	A1	20020307	WO 2001US27142	A	20010830	200252	B
AU 200188585	A	20020313	AU 200188585	A	20010830	200252	
US 20020025340	A1	20020228	US 2000229085	A	20000830	200252	
			US 2001943138	A	20010830		

Priority Applications (No Type Date): US 2000241636 P 20001019; US 2000229085 P 20000830; US 2000229989 P 20000905; US 2001943138 A 20010830

Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200217816 A1 E 27 A61F-002/00
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
AU 200188585 A A61F-002/00 Based on patent WO 200217816
US 20020025340 A1 A61K-009/14 Provisional application US 2000229085
Abstract (Basic): WO 200217816 A1

NOVELTY - A biphasic injectable composition comprises a solid polymer phase and a carrier substrate phase.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for tissue augmentation by injecting the biphasic injectable composition.

USE - As solid injectable materials for soft tissue volume replacement. The composition is used as a material in plastic and reconstructive surgery, for soft tissue augmentation (functional or aesthetic purposes) in urethra, vocal cords or other urological tissue sites, for treating stress incontinence. A single phase composition such as PVP are useful for effacing fine rhytids, such as crows feet, depressed acne scars, perioral rhytids, stretch marks and furrows.

ADVANTAGE - The novel composition is safe, predictable, permanent or may be resorbed by the body, resistant to infection, resistant to extrusion and non-antigenic. The compositions are moldable following implantation, but stable after remolding, and mimic the consistency of the tissue that it replaces. The composition is permanent or semi-permanent, biocompatible, moldable, and mechanically stable with respect to the surrounding tissues, hence suitable for use in soft tissue augmentation. The compositions comprising Gore-Tex (e-PTFE) provides a stable implant. The textured microparticles in the compositions provides a more lasting implant result. The composition comprising Gore-Tex particles provides limited fibrous tissue in growth into the surface of the material, thereby provides early stabilization, while allowing for removal if necessary. Gore-Tex is inert and does not change shape or reabsorb with time, non-carcinogenic, rarely allergenic, and causes only minimal tissue reaction. The size of the particles prevents the material from being phagocytozed, and thus, it does not serve as an antigen. Histology demonstrated that hypersensitivity granuloma formation does not occur and that only macrophages and mature collagen are present over time. PVP is an inert water-soluble polyamide, which does not act as a skin or eye irritant or as a skin-sensitizer. Hence, PVP is well tolerated by parenteral administration for **plasma** volume expansion.

pp; 27 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: The solid polymer phase is made from micronized expanded polytetrafluoroethylene (e-PTFE) particles, polydioxanone, long chain aliphatic polymers Nylon 6, long chain aliphatic polymers Nylon 6,6, polypropylene, copolymer made from 90% glycolide and 10% L-lactide, silk, poly epsilon-caprolactone, polylactide, polyglycolide, poly lactide-co-glycolide, polyhydroxy valerate, biocompatible micronized polyethylene, bioactive glass particulate, synthetic bone graft

particulate, and/or polyhydroxy valerate, preferably e-PTFE. The solid polymer phase comprises micronized e-PTFE having size of 65-1000 **micron** .

ORGANIC CHEMISTRY - Preferred Materials: The carrier substrate phase is polyvinylpyrrolidone (PVP), silicone oil, gelatin, collagen, fat, hyaluronic acid, saline, water or **plasma** . The carrier substrate phase comprises micronized polydioxanone particles having size of 65-1000 **micron** . Preferred Properties: The e-PTFE particles has size of 65-1000 **micron** . The PVP has K value of 12-100, preferably 17.

PHARMACEUTICALS - Preferred Composition: The composition contains the solid polymer phase comprising e-PTFE, and the carrier substrate comprising PVP at a ratio of 3:2 (PVP/e-PTFE) by weight

Extension Abstract:

ADMINISTRATION - A delivery apparatus containing the biphasic injectable composition is injected subcutaneously, **intradermally** , intramuscularly, by periurethral injection or injecting the vocal cords, into the injection site.

Derwent Class: A96; D22; P32
International Patent Class (Main): A61F-002/00; A61K-009/14
International Patent Class (Additional): A61F-002/02; A61K-031/728; **A61K-038/17**

9/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
016058308
WPI Acc No: 2004-216159/200421
Use of guanylhydrazones for inhibition of CD83 molecules in dendritic cells in organ transplantation techniques

9/26,TI/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015862960
WPI Acc No: 2004-020791/200402
Preparation of stable microparticles of a water-insoluble or poorly soluble compound useful in pharmaceutical industry involves applying energy to mixture of the water-insoluble or poorly soluble compound, phospholipid and surfactant

9/26,TI/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015850232
WPI Acc No: 2004-008059/200401
Composition useful for treating diabetes, hyperglycemic disorders e.g. obesity, increased cholesterol, and kidney related disorders comprises new and known diphenylethylene compounds

9/26,TI/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
015769065
WPI Acc No: 2003-831267/200377
Use of estriol for the prevention of myocardial ischemia/for the treatment of coronary vasospasm/for the reduction of coronary artery reactivity

9/26,TI/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015719263
WPI Acc No: 2003-781463/200374
Method for the modulation of neoplastic growth in colon cancer, comprises administration of a combination of chromen-4-one derivative, its salt or ester, and a non-steroidal antiinflammatory drug

9/26,TI/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015714019
WPI Acc No: 2003-776219/200373
Treatment of e.g. hyperuricemia involves use of a composition comprising (-) enantiomer of (3-trihalomethylphenoxy)(4-halophenyl)acetic acid derivative

9/26,TI/8 (Item 8 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015555935
WPI Acc No: 2003-618090/200358
Composition for the treatment of e.g. peripheral arterial occlusive disease and coronary restenosis comprises multifunctional phosphodiesterase inhibitor and adenosine reuptake inhibitor

9/26,TI/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015310947
WPI Acc No: 2003-371882/200335
Composition for reducing transfer of cholesteryl ester between high density lipoproteins and low density lipoproteins, and for treating cardiovascular diseases, comprising sterol or stanol derivative

9/26,TI/10 (Item 10 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015149828
WPI Acc No: 2003-210355/200320
Producing a purified cluster of differentiation CD4+ Th2 lymphocyte population, for treating an autoimmune disease, comprises contacting a CD4+ T cell population with antibodies to CD3 and to a T cell costimulatory molecule

9/26,TI/11 (Item 11 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015087061
WPI Acc No: 2003-147579/200314
Isolated polynucleotide for encoding polypeptides used to diagnose and treat electrolyte disorders leading to renal disease, e.g. Paget's disease, hypercalcemia and sarcoidosis

9/26,TI/12 (Item 12 from file: 350)
DIALOG(R)File 350:Derwent WPIX

(c) 2004 Thomson Derwent. All rts. reserv.
014886168
WPI Acc No: 2002-706874/200276
Treatment of a hematologic tumor or malignancy e.g. multiple myeloma, involves administering the use of a G1 and/or S phase drug, or its derivative or analog

9/26,TI/13 (Item 13 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014876387
WPI Acc No: 2002-697093/200275
New targeting molecule useful for delivering enzyme inhibitor into non-polarized epithelial cells of patient afflicted with disease associated with non-polarized epithelial cells, linked to enzyme inhibitor

9/26,TI/15 (Item 15 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014789564
WPI Acc No: 2002-610270/200266
Pharmaceutical composition for treating systemic inflammatory response syndrome, sepsis, septic shock and/or thrombus formation in microvasculature in mammals, comprises a partial inhibitor of factor VIII

9/26,TI/16 (Item 16 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014787730
WPI Acc No: 2002-608436/200265
New lymphocyte function associated antigen antagonist compound useful for treating, e.g. arthritis, psoriasis, meningitis, encephalitis, autoimmune diseases, central nervous system inflammatory disorder or atherosclerosis

9/26,TI/17 (Item 17 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014686504
WPI Acc No: 2002-507208/200254
A novel complement activation inhibitor (monoclonal antibody (MAb) 137-76 or MAb 137-30) which binds to C5 and inhibits type II endothelial cell activation, useful for treating delayed xenograft rejection or acute vascular rejection

9/26,TI/18 (Item 18 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014541752
WPI Acc No: 2002-362455/200239
Use of cannabinoid and resorcinolic compounds to inhibit aggregation of blood platelets

9/26,TI/19 (Item 19 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2004 Thomson Derwent. All rts. reserv.
014494576

WPI Acc No: 2002-315279/200235
New adjuvant compound useful for enhancing immune responses in animal

9/26,TI/20 (Item 20 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014396444
WPI Acc No: 2002-217147/200227
Method for increasing apolipoprotein E in plasma and tissues of a mammal involves the use of a combination of farnesoid X activated receptor (FXR) and liver X receptor (LXR)

9/26,TI/21 (Item 21 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014358436
WPI Acc No: 2002-179137/200223
Treatment of an inflammation reaction e.g. skin sunburn in a subject involves the use of 2,4,6-trihydroxy-alpha-para-methoxyphenylacetophenone or its derivative

9/26,TI/22 (Item 22 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014350974
WPI Acc No: 2002-171677/200222
Composition useful for treatment of cardiovascular diseases such as restenosis comprises re-endothelialization promoter and a lipoprotein oxidation inhibitor

9/26,TI/23 (Item 23 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014052207
WPI Acc No: 2001-536420/200159
Modified ligand for treatment or prophylaxis of conditions associated with a target receptor contains conjugation agent that is reactive with moiety of the receptor to which the parent ligand binds and is covalently attached to the moiety

9/26,TI/24 (Item 24 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013843951
WPI Acc No: 2001-328164/200134
New aromatic compounds are liver glycogen phosphorylase inhibitors, for treating e.g. diabetes (especially type 2 diabetes), obesity, hypertension and hyperlipidemia, and inhibiting glucose production

9/26,TI/25 (Item 25 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013805636
WPI Acc No: 2001-289848/200130
New recombinant DNA encoding CD28 useful for diagnosing and treating immune-mediated diseases, infections or disorders, e.g. systemic lupus

erythematosus, asthma, transplant rejection, rheumatoid arthritis

9/34/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016011015 **Image available**
WPI Acc No: 2004-168866/200416
Administration of substance e.g. hormones such as insulin, into mammal comprises injecting the substance intradermally through microneedles
Patent Assignee: PINKERTON T C (PINK-I)
Inventor: PINKERTON T C
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20040028707	A1	20040212	US 2001897801	A	20010629	200416 B
			US 2003443361	A	20030522	

Priority Applications (No Type Date): US 2001897801 A 20010629; US 2003443361 A 20030522
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20040028707	A1		26	A61K-009/00	Cont of application US 2001897801

Abstract (Basic): US 20040028707 A1

NOVELTY - A pharmaceutical substance is administered to a mammal by injecting the substance **intradermally** through one or more **microneedles** having length and **outlet** for selectively delivering the substance into the dermis to obtain absorption of the substance in the dermis.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a microneedle for **intradermal** injection of pharmaceutical substance, comprising and outlet for delivering the substance into the dermis.

USE - For delivering hydrophobic or hydrophilic substance, e.g. hormone such as insulin and PTH, or nucleic acid, to **intradermal** space of a mammal.

ADVANTAGE - The inventive method improves the systemic absorption relative to that obtained upon subcutaneous administration of the substance. It improves pharmacokinetics or increases the bioavailability of the substance.

DESCRIPTION OF DRAWING(S) - The drawing shows a timework of **plasma** insulin levels of **intradermal** versus subcutaneous bolus administration of fast-acting.

pp; 26 DwgNo 1/11
Technology Focus:

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The administering is through at least one small gauge hollow needle. The needle is inserted to the depth, which delivers the substance 0.3-2 **mm** below the surface. The administering comprises inserting the needle into the skin to a depth of 0.3-2 **mm** . The needle(s) are inserted perpendicularly to the skin.

Preferred Parameters: The improved pharmacokinetics comprises a decrease in Tmax, and increase in Cmax. The improved pharmacokinetics comprises a decrease in T(lag) and in k(a). The substance is administered over a not more than10 minutes. The substance is administered as a solution in an amount of 1-2000 (preferably 1-300) nL. The substance has molecular weight approximately1000 Daltons.

Preferred Device: The microneedle is contained in an array of 3-6 microneedles. The **needle** has an **outlet** with an exposed height of

0-1 **mm** . The **microneedle** has **outlet** of 0-1 **mm** and length of 0.5-1.7 **mm** . It is 30-34 gauge needle.

Derwent Class: B04; B07; D16; P34
International Patent Class (Main): A61K-009/00
International Patent Class (Additional): A61M-031/00

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File 348:EUROPEAN PATENTS 1978-2004/May W04
File 349:PCT FULLTEXT 1979-2002/UB=20040527,UT=20040520
Set     Items   Description
S1      15653   INTRADERMAL? OR INTRA()DERMAL? OR INTRAEPIDERMAL? OR INTRA-
             ()EPIDERMAL?
S2      72919   NEEDLE? ? OR MICRONEEDLE? ?
S3     159351   OUTLET? ?
S4     981258   MM OR MILLIMETER? ? OR MILLIMETRE? ? OR UM OR MICRON? ? OR
            MICROM? ? OR MICROMETER? ? OR MICROMETRE? ?
S5     115416   PLASMA
S6      39974   IC=(A61M031 OR A61M-037 OR A61M-005 OR A61K-000 OR A61K-03-8)
S7         70   (S1 OR S2(3N)S3)(S)S4(S)S5
S8         19   S6 AND S7
S9          0   (S1/TI AND S7) NOT S8

 8/6/1      (Item 1 from file: 348)
01216623
MODULATION OF VASCULAR PERMEABILITY BY MEAN OF TIE2 RECEPTOR ACTIVATORS

 8/6/5      (Item 4 from file: 349)
01049775
TREATMENT OF METABOLIC DISORDERS WITH A TNF RECEPTOR FAMILY MEMBER (FRADJ
    AND/OR CRYPTIC) AGONISTS OR ANTAGONISTS

 8/6/6      (Item 5 from file: 349)
01001217     **Image available**
ALBUMIN FUSION PROTEINS

 8/6/10      (Item 9 from file: 349)
00883877
NUCLEIC ACID AND CORRESPONDING PROTEIN NAMED 158P1H4 USEFUL IN THE
    TREATMENT AND DETECTION OF BLADDER AND OTHER CANCERS

 8/6/12      (Item 11 from file: 349)
00853584     **Image available**
USE OF INHIBITORS OF PLACENTAL GROWTH FACTOR FOR THE TREATMENT OF
    PATHOLOGICAL ANGIOGENESIS, PATHOLOGICAL ARTERIOGENESIS, INFLAMMATION,
    TUMOUR FORMATION AND/OR VASCULAR LEAKAGE

 8/6/13      (Item 12 from file: 349)
00830708
MATERIALS AND METHODS INVOLVING HYBRID VASCULAR ENDOTHELIAL GROWTH FACTOR
    DNAs AND PROTEINS AND SCREENING METHODS FOR MODULATORS

 8/6/15      (Item 14 from file: 349)
00748439     **Image available**
METHODS AND REAGENTS FOR DETERMINING ENZYME SUBSTRATE SPECIFICITY, AND USES
    RELATED THERETO

 8/6/16      (Item 15 from file: 349)
00547655
ANTI-INFLAMMATORY PEPTIDES DERIVED FROM IL-2 AND ANALOGUES THEREOF

 8/6/17      (Item 16 from file: 349)
00541880
ANTAGONISTS SPECIFIC FOR THE CORTICOTROPIN-RELEASING FACTOR RECEPTOR TYPE 2
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(CRFR2)

8/3,AB,K/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

01114591
TREATMENT OF HYPERSENSITIVITY CONDITIONS
TRAITEMENT D'ETATS D'HYPERSENSIBILITE
Patent Applicant/Assignee:
THE UNIVERSITY OF QUEENSLAND, BRISBANE, Queensland 4072, AU, AU (Residence), AU (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
SHIELS Ian Alexander, 17 Sherlock Road, Muilea Road, MUIRLEA, Queensland 4306, AU, AU (Residence), AU (Nationality), (Designated only for: US)
TAYLOR Steven Maxwell, 17 Perdita Street, BELLBIRD PARK, Queensland 4300, AU, AU (Residence), AU (Nationality), (Designated only for: US)
FAIRLIE David, 73 Trevallyan Drive, SPRINGWOOD, Queensland 4127, AU, AU (Residence), AU (Nationality), (Designated only for: US)
Legal Representative:
GRIFFITH HACK (agent), 509 St Kilda Road, MELBOURNE, Victoria 3004, AU,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200435080 A1 20040429 (WO 0435080)
Application: WO 2003AU1374 20031016 (PCT/WO AU03001374)
Priority Application: AU 2002952129 20021017
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 10033
English Abstract
This invention relates to methods of treatment of hypersensitivity conditions such as asthma and other allergic conditions, and especially to treatment of these conditions with cyclic peptidic and peptidomimetic compounds which have the ability to modulate the activity of G protein-coupled receptors. The compounds preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes and macrophages. Particularly preferred compounds for use in the methods of the invention are disclosed.
Main International Patent Class: **A61K-038/08**
International Patent Class: **A61K-038/12** ...
Fulltext Availability: Claims
Claim
... human PMNs, isolated as previously described (Sanderson et al, 1995), using a buffer of 50 **mM** HEPES, 1 **mM** CaC12, 5 **mM** MgC12, 0.5% bovine serum albumin, 0.1% bacitracin and 100 @iM phenylmethylsulfonyl fluoride (PMSF...leakage into the dermis. Figure I shows the optical density of dermal punch extracts following **intradermal** injection of rabbit anti-chicken ovalbumin at 0-400 gg site-' following pretreatment with AcF...

...orally or topically. Data are shown as absorbance at 650nm as a percentage of the **plasma** absorbance, as mean values 1 SEM (n=3-6). *indicates a P value < 0.05...
...the tissues and migration of these cells away from blood vessels. Figure 3 shows that **intradermal** injection of increasing amounts - 22 of antibody leads to a dose-responsive increase in the pathology index scored by dermal samples (A). Data are shown for dermal samples **intradermally** injected with saline or 400 gg antibody per site (n=S) in rats pretreated with...

8/3,AB,K/3 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

01114590
TREATMENT OF OSTEOARTHRITIS
TRAITEMENT DE L'ARTHROSE
Patent Applicant/Assignee:
THE UNIVERSITY OF QUEENSLAND, Brisbane, Queensland 4072, AU, AU (Residence), AU (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
SHIELS Ian Alexander, 17 Sherlock Road, Muirlea Road, Muirlea, Queensland 4306, AU, AU (Residence), AU (Nationality), (Designated only for: US)
TAYLOR Steven Maxwell, 17 Perdita Street, Bellbird Park, Queensland 4300, AU, AU (Residence), AU (Nationality), (Designated only for: US)
Legal Representative:
GRIFFITH HACK (agent), 509 St Kilda Road, Melbourne, Victoria 3004, AU,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200435079 A1 20040429 (WO 0435079)
Application: WO 2003AU1373 20031016 (PCT/WO AU03001373)
Priority Application: AU 2002952086 20021016
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 9626
English Abstract
This invention relates to methods of treatment of osteoarthritis, and especially to treatment of this condition with cyclic peptidic and peptidomimetic compounds which have the ability to modulate the activity of G protein-coupled receptors. The compounds preferably act as antagonists of the C5a receptor, and are active against C5a receptors on polymorphonuclear leukocytes and macrophages. Particularly preferred compounds for use in the invention are disclosed.
Main International Patent Class: **A61K-038/08**
International Patent Class: **A61K-038/12** ...
Fulltext Availability: Claims
Claim
... human PMNs, isolated as previously described (Sanderson et al, 1995), using a buffer of 50 **mM** HEPES, I **mM** CaC12, 5 **mM** M9C12,

0.5% bovine serum albumin, 0.1% bacitracin and 100 pM phenylmethylsulfonyl fluoride (PMSF...leakage into the dermis. Figure 1 shows the optical density of dermal punch extracts following **intradermal** injection of rabbit anti-chicken ovalbumin at 0-400 gg site-' following pretreatment with AcF...
...orally or topically. Data are shown as absorbance at 650nm as a percentage of the **plasma** absorbance, as mean values 1 SEM (n=3-6). *indicates a P value < 0.05...
...the tissues and migration of these cells away from blood vessels. Figure 3 shows the **intradermal** injection of increasing amounts of antibody leads to a dose-responsive increase in the pathology index scored by dermal samples (A). Data are shown for dermal samples **intradermally** injected with saline or 400 gg site-' antibody (n=5) in rats pretreated with AcF...
...determined by scoring the animal's gait, measuring joint swelling, and determination of synovial and **plasma** cytokine TNF-a levels. The rats are euthanased 8 weeks after the commencement of the...
...clinical examination of joints to determine joint pain and range of movement, and clinical biochemistry (**plasma** electrolytes - Na+, K+, Ca2+1 liver enzymes, pancreatic enzymes, creatinine, blood urea nitrogen and glucose...
...to proteolytic degradation for at least several hours at 37'C in human blood or **plasma** , in human or rat gastric juices, or in the presence of digestive enzymes such as...
...bioavailable as drugs than acyclic peptides, which can rarely be 10 administered orally. Fourthly, the **plasma** half-lives of cyclic molecules are usually longer than those of peptides. It will be...

8/3,AB,K/4 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01103321
METHOD AND APPARATUS FOR EPIDERMAL DELIVERY OF A SUBSTANCE
PROCEDE ET APPAREIL DESTINES A ADMINISTRER UNE SUBSTANCE PAR VOIE EPIDERMIQUE
Patent Applicant/Assignee:
BECTON DICKINSON AND COMPANY, 1 Becton Drive, Franklin Lakes, NJ 07417-1880, US, US (Residence), US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
HAIDER M Ishaq, 204 Ketrick Court, Morrisville, NC 27560, US, US (Residence), US (Nationality), (Designated only for: US)
CLARKE Richard P, 5000 Swift Ridge Road, Raleigh, NC 27606, US, US (Residence), US (Nationality), (Designated only for: US)
FENTRESS James K, 500 Golden Horseshoe Circle, Apt. B, Morrisville, NC 27560, US, US (Residence), US (Nationality), (Designated only for: US)
MIKSZTA John A, 3205 Lochinvar Drive, Durham, NC 27705, US, US (Residence), US (Nationality), (Designated only for: US)
MARTIN Frank E, 2807 Burton Road, Durham, NC 27704, US, US (Residence), US (Nationality), (Designated only for: US)
Legal Representative:

WEST Robert E (agent), Becton Dickinson and Company, 1 Becton Drive, Franklin Lakes, NJ 07417-1880, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200424219 A1 20040325 (WO 0424219)
Application: WO 2003US28273 20030910 (PCT/WO US03028273)
Priority Application: US 2002409193 20020910
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 7403
English Abstract
A methbd and apparatus for epidermal and/or **intradermal delivery** of a substance is provided. A **needle** having at least one side port is used to penetrate the skin of a subject. The needle may be of any size. A substance is delivered through the side port and into the skin. The side port can be of any size or shape and be arranged at any location on the needle.
Main International Patent Class: **A61M-005/32**
Fulltext Availability: Detailed Description
Detailed Description
... substances.
[0007] Some groups have reported on systemic administration by what has been characterized as " **intradermal** " injection. In one such report, a comparison study of subcutaneous and what was described as " **intradermal** " injection was performed (Autret et al, Therapie 46:5-8, 1991). The pharmaceutical substance tested...
...Although it was stated that the drug was injected intradennally, the injections used a 4 **mm** needle pushed up to the base at an angle of 60'. This would have resulted in placement of the injectate at a depth of about 3.5 **mm** and into the lower portion of the reticular dermis or into the subcutaneous tissue rather...
...subcutaneous and what was characterized as intraden-nal administration, in the times at which maximum **plasma** concentration was reached, the concentrations at each assay time and the areas under the curves...

8/3,AB,K/18 (Item 17 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2004 WIPO/Univentio. All rts. reserv.
00521703
THERAPEUTIC AGENT FOR NGF
AGENT THERAPEUTIQUE POUR NGF
Patent Applicant/Assignee:
UNIVERSITY OF BRISTOL,
ROBERTSON Alan George Simpson,
ALLEN Shelley Jane,
DAWBARN David,
Inventor(s):

ROBERTSON Alan George Simpson,
ALLEN Shelley Jane,
DAWBARN David,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9953055 A2 19991021
Application: WO 99GB1108 19990409 (PCT/WO GB9901108)
Priority Application: GB 987781 19980409
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 13156
English Abstract
This invention relates to the use of a domain of Trk as a therapeutic agent and for screening purposes and rational design of NGF mimetics.
...International Patent Class: **A61K-038/17**
Fulltext Availability: Detailed Description
Detailed Description
... is not able to do this.
In Vivo Effects of TrkAIg-like domains: Inhibition of **Plasma** Extravasation
Inhibition of NGF activity in vivo
All in vivo experiments were carried out according to the Animals (Scientific Procedures) Act 1986 under terminal anaesthesia. **Plasma** protein extravasation in rat skin induced by **intradermal** (i.d.) NGF was measured by the extravascular accumulation of intravenous (i.v.) 1251-human...
...allowed over a 30 min period. A blood sample was taken by cardiac puncture (for **plasma**) and the rats killed by cervical dislocation. The dorsal skin was then removed and injection sites punched out (16 **mm** diameter). **Plasma** and skin sites were counted in a gamma counter. The **plasma** protein extravasation at each site was expressed as volume of **plasma** extravasated...

8/3,AB,K/19 (Item 18 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2004 WIPO/Univentio. All rts. reserv.
00477349
COMPLEXES OF APOLIPOPROTEIN E AND CILIARY NEUROTROPHIC FACTOR (CNTF) AND METHODS OF USE
COMPLEXES D'APOLIPOPROTEINE E ET DU FACTEUR CILIAIRE NEUROTROPHIQUE (CNF) ET MODES D'UTILISATION
Patent Applicant/Assignee:
DUKE UNIVERSITY,
MATTHEW William D,
STRITTMATTER Warren J,
GUTMAN Catherine R,
Inventor(s):
MATTHEW William D,
STRITTMATTER Warren J,
GUTMAN Catherine R,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9908701 A1 19990225

Application: WO 98US17208 19980819 (PCT/WO US9817208)
Priority Application: US 9756605 19970820
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English Abstract

Provided herein are compositions comprising complexes of apolipoprotein E and ciliary neurotrophic factor. The apolipoprotein E can be any isoform, but is preferably apolipoprotein E3. Also preferred are covalent complexes of apolipoprotein E and ciliary neurotrophic factor, more preferably those formed by intermolecular disulfide bonds between cysteine residues. Further provided are methods of enhancing the survival of neural cells by administering a composition comprising a complex of apolipoprotein E and ciliary neurotrophic factor. The claimed methods can be carried out both i(in vitro) and i(in vivo).

Main International Patent Class: **A61K-038/18**
...International Patent Class: **A61K-038/18** ...
... **A61K-038/17**
Fulltext Availability: Claims
Claim
... of administration may be employed, including administration by parenteral injection (e.g., subcutaneous, intramuscular, or **intradermal**), or by oral, rectal, topical, nasal, ophthalmic, intrathecal, and intracerebral administration. The apoE:CNTF complexes...
...in vivo dosage of apoE:CNTF complexes administered will be sufficient to result in peak **plasma** concentration of the complex of from about lxlO-1, 1 x 100 or I x...Blotto. After probing the membranes with anti-CNTF antibody, the membranes were stripped in 200 **mM** glycine-HCL with 0.05% Tween, pH 2.5, at 80'C for one hour...

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...consequently 17-OH progesterone **plasma levels** are increased while **plasma** 11-deoxycortisol...shown [1,2, 3] that elevated **plasma levels** of 21-deoxycortisol could also...Zealand rabbits by multiple **intradermal injections** of the antigen in Freund's adjuvant...
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